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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

November 20, 1997

MEMORANDUM

SUBJECT: EFED's Section 3 Registration Eligibility Decision Chapter for Fipronil Use on Corn

FROM: James A. Hetrick, Ph. D., Soil Chemist James A. Hetrick 11/20/97
Brian Montague, Biologist
Gail Maske, Chemist
Edward Odenkirchen, Ph.D., Chemist 11/20/97

THRU: Arnet Jones, Branch Chief 11/20/97
Environmental Risk Branch 1
Environmental Fate and Effects Division (7507C)

TO: Susan Lewis, PM 71
Registration Division (7505C)

Attached is EFED's completed chapter for the Section 3 registration of fipronil for in-furrow use on corn. Included in this package is a copy of our letter of Nov. 14 (hand-delivered) that summarizes our ecological risk characterization for this use of fipronil.

Please contact Jim Hetrick (305-5237) or Gail Maske (305-5245) if you have any questions.

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TO: Susan Lewis, PM 71
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EFED has reviewed the environmental fate and ecotoxicology studies and other information provided to support the registration of fipronil 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)-phenyl)-4-((1,R,S)-(trifluoromethyl) sulfinyl)-1-H-pyrazole-3-carbonitrile for in furrow use on corn. The environmental fate and ecological effects data are generally sufficient to enable a risk assessment and risk characterization for in furrow use on corn. In furrow application of fipronil is likely to reduce ecological exposure. EFED believes, however, that future uses of fipronil that are not soil-incorporated are likely to pose higher risks to nontarget organisms.

The environmental fate data for fipronil are generally acceptable to formulate a comprehensive fate and transport assessment. However, a major limitation in the fipronil environmental fate assessment is the low confidence level associated with data on the persistence of fipronil in aquatic environments. The absence of conclusive persistence data forces an assumption of high persistence for environmental fate and transport modeling . This may lead to higher estimates of the concentration of fipronil and it's degradates in surface water which may impact drinking water and aquatic risk assessments. Soil and aquatic metabolism studies provide contradictory data on fipronil persistence to microbially-mediated degradative processes. The registrant should provide a complete explanation on disparate half-lives reported for fipronil in aquatic and soil metabolism studies. The environmental fate assessment for fipronil metabolites is more tentative because of the lack persistence data in terrestrial and aquatic environments. Submission of soil and aquatic metabolism studies on the individual metabolites would provide a more reliable and comprehensive fate assessment.

Fipronil is moderately persistent to persistent ($t_{1/2}$= 128 to 300 days) and relatively immobile (mean K_{oc} 727 mL/g) in terrestrial environments. In aquatic environments, the environmental behavior of fipronil is more tentative because soil and aquatic metabolism studies provide contradictory data on fipronil persistence to microbially-mediated degradative processes. Major routes of dissipation appear to be dependant on photodegradation in water, microbially-mediated degradation, and soil binding. Fipronil degrades to form MB46136 5-amino-1-(2,6-dichloro-4-trifluoro methylphenyl)-3-cyano-4-trifluoromethyl-sulphonyl-pyrazole and RPA 200766 (5-amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methanesulfinyl pyrazole in aerobic soil metabolism studies. MB46513 (5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-4-trifluoro-methylpyrazole is a major degradate in photolysis studies. MB45950 (5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoro-methyl-thio-pyrazole) appears to be predominantly formed under low oxygen conditions from microbial-mediated processes. These degradates appear to be persistent and relatively immobile in terrestrial and aquatic environments.

Ecological risk issues from the in furrow use of fipronil, formulated as REGENT 1.5G, 3G, 80WG and 4SC, on corn are associated with ingestion of exposed granular fipronil by gallinaceous birds (*i.e.*, bobwhite quail and pheasant) and the high toxicity of fipronil and its degradates to aquatic invertebrates in estuarine systems. Fipronil and its associated degradates did not exceed acute toxic levels of concern for small mammal species, freshwater fish, or freshwater invertebrates. Fipronil degrades to form metabolites of potential toxicological concern (MB46136, MB46513, RPA 200766, and MB45950). These metabolites are assumed to be equally toxic as parent fipronil because they contain the same toxic moiety (CF_3-) as fipronil. In addition, the Agency has reviewed acute toxicity studies with 3 of these degradates (excluding RPA 200766) that indicate they will display higher toxicity to non-target organisms than the parent compound. Environmental fate data indicate that fipronil metabolites are persistent ($t_{1/2}$>600 days) and relatively immobile. Because of the high environmental persistence, there is a high potential for accumulation in terrestrial environments and in aquatic environments when fipronil reaches water. Accumulation of fipronil residues (particularly fipronil degradates) are likely to cause long-term ecological exposure. In furrow application of fipronil with soil incorporation , however, is expected to reduce direct exposure to fipronil granules and to reduce the amount of fipronil which moves in runoff waters.

The ecological effects data are insufficient for a comprehensive ecological effects assessment for in furrow fipronil use on corn. Because fipronil is extremely toxic to estuarine invertebrates and refined surface water modeling indicates surface water concentrations in excess of toxicity thresholds, a new mysid full lifecycle (72-4) study with MB 46136 is needed to assess chronic effects on non-target aquatic invertebrates. Additionally, since fipronil metabolites (MB46136 and MB45950) contains the toxicological moiety (CF_3-) of parent fipronil and long-term exposure is anticipated because of high persistence in terrestrial environments, avian dietary studies are needed for MB46136 and MB45950. Also, since fipronil and its metabolites contain the same toxic moiety (CF_3-) and are persistent, a full fish life cycle study (72-5) is needed to assess cumulative toxicological impact on fish.

Other data requirements for refined ecological effects assessment of above ground uses are avian reproduction study (71-4) with bobwhite quail at maximum expected concentrations, honey bee acute contact LD_{50} study (141-1), and honey bee toxicity of residues on foliage (141-2). Although the avian reproduction study and honey bee studies are not needed to support in furrow fipronil use on corn, they will be needed to support above ground uses of fipronil. These studies should be conducted at the highest application rate for prescribed fipronil uses and should be conditionally required for continued registration.

Because ground and surface water monitoring data are not available, drinking water concentrations for fipronil and its degradates are based solely on ground and surface water models. Acute and chronic drinking water concentrations for fipronil in surface water are not likely to exceed 0.715 and 0.276 µg/L, respectively. Based on the GENEEC model, acute and chronic drinking water concentrations of fipronil metabolites in surface water are respectively 0.168 and 0.062 µg/L for MB 46136, 0.014 and 0.009 µg/L for MB 46513, and 0.039 and 0.019 µg/L for MB 45950. Further refinement using a 36 year PRZM-EXAMS simulation suggest fipronil metabolites can potentially accumulate in surface water from 0.005 to 3.9 µg/L for MB 46513, 0.004 to 2.3 µg/L for MB45950, and 0.004 to 0.89 µg/L for MB46136.

Based on the SCI-GRO model, acute drinking water concentrations in shallow ground water on highly vulnerable sites are not likely to exceed 0.055 µg/L for parent fipronil, 0.001 µg/L for MB 46136, 0.00026 µg/L for MB 46513, and 0.00036 µg/L for MB 45950. Because fipronil residues are moderately persistent to persistent in terrestrial environments, chronic concentrations of fipronil residues are not expected to be higher than acute values. Because fipronil and its metabolites exhibit persistence and lower sorption affinity on coarse textured soils with low organic matter content, it possible that fipronil and it metabolites can move into shallow ground water on vulnerable sites. Several highly vulnerable areas for shallow ground water have been identified as the coastal plains of Georgia, South Carolina, and North Carolina; eastern shore region of Lake Ontario; and the Delmarva Peninsula area. A review of the available NAWQA data concerning the intensity of land use for grain corn indicate that a number of counties within the Delmarva Peninsula, in vulnerable regions of North Carolina, and the eastern shore region of Lake Ontario are very intensively planted in grain corn (greater than 50,000 acres/county). In addition, more limited areas in Georgia and South Carolina are intensively planted in grain corn with 25,000 to 50,000 acres planted per county. Because several of these vulnerable areas are adjacent to estuarine environments, highly sensitive estuarine ecosystems may be potentially exposed to fipronil residues through surface water runoff or ground -surface water interactions.

<u>Proposed Mitigation</u>

Recommended mitigation options for in furrow use of fipronil are (1) restricted use classification and (2) label advisories. The registrant has volunteered to delete T-Band application methods from this proposed use to further mitigate risks to avian species.

Fipronil meets the criteria for classification as a **Restricted Use Pesticide** with regard to risks to estuarine invertebrates and birds (40 CFR 152.170 (c)(1)(iii)), and with regard to an avian acute oral toxicity value less than 50 mg/kg for a granular product (LD_{50} for Bobwhite Quail= 11.3

mg/kg) (40 CFR 152.170 (c)(2)(I)). EFED therefore recommends that fipronil be classified as a Restricted Use Pesticide.

Labels currently proposed contain language which is not consistent among products. EFED recommends that the label advisories for the environmental hazards statement for REGENT 1.5G, 3G, 80WG and 4SC use on corn should be consistent and include:

> This pesticide is toxic to birds, fish, and aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Cover, incorporate or clean up granules that are spilled. Do not contaminate water when disposing of equipment washwater or rinsate.

Because of EFED's concern for estuarine organisms and because of the potential for accumulation of toxic residues in surface water receiving runoff from treated fields, EFED also recommends that the following precautions be incorporated into label language:

Observe the following precautions when applying in the vicinity of aquatic areas:

> Do not apply within 20 yards of lakes, reservoirs, rivers, permanent streams, marshes, natural ponds, estuaries, commercial aquaculture facilities, or other bodies of water that convey water to these areas. (It is our understanding that this is consistent with the buffer established for corn cluster insecticides.)

> Protection of aquatic areas may be enhanced by maintaining all or a portion of this buffer in vegetative cover.

Environmental fate data suggest that fipronil and particularly its degradates are persistent in the environment. PRZM/EXAMS modeling incorporating these data incates that under the proposed application to corn, fipronil and its degradates have the potential to accumulate in soil and surface water over multiple consecutive years of application. This can result in concentrations exceeding those estimated for the first year of application. Although these predictions are not highly refined, they do suggest that risks to aquatic organisms may increase over multiple consecutive years of application. Because of persistence and possible accumulation of residues, EFED recommends that labels for all fipronil products registered for use on corn indicate that fipronil should not be applied to the same field in consecutive years. Alternating years of application may provide sufficient time for degradative processes to reduce the potential for residue accumulation in the environment.

ECOLOGICAL RISK BRANCH I REVIEW

A. Review Information:

Type: Section 3 Application on Corn; nationwide
Barcode: D236430, D236432, D237516, D228555, D237727, D236394, D237516, D237517, D236956, D239710
Chemical Name: Fipronil: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((1,R,S)-(trifluoromethyl) sulfinyl)-1-H-pyrazole-3-carbonitrile
Chemical Type: Phenylpyrazole insecticide
CAS #: 120068-37-3
PC Code: 129121
Active Ingredient Name: Fipronil
Product Trade Names: Regent 80 WG, Regent 1.5G, Regent 3.0 G, and Regent 4SC Insecticides.

Submission and Label Information

Section 3 Registration of four new products containing the active ingredient fipronil on field corn.

Use Characterization for Corn Use Pesticides

According to Agricultural Statistics, 1994 (USDA) over 73 million acres of corn were planted in 1993 in 47 states (Alaska, Hawaii, Rhode Island excluded). Seed corn is also produced in Hawaii to increase breeder lines, but the acreage for this purpose is not quantified by the available data. Much of the corn belt includes ecologically sensitive ecosystems. A majority of the corn acreage (70%) is found in the following 13 states; Ohio, Indiana, Illinois, Michigan, Wisconsin, Minnesota, Iowa, Missouri, Kansas, Nebraska, Colorado, North Dakota, and South Dakota. Another 15% is grown in the southeastern states. A significant portion of the corn acreage occurs in such wildlife rich areas as the Prairie Pothole region, the Sandhills lake region of Nebraska and the playa lakes areas in the southwest. Many corn growth areas are used by waterfowl and shorebirds as breeding, feeding and migratory resting grounds, and they support a significant proportion of the total population of these birds. A number of freshwater habitat types are potentially exposed to varying levels of pesticide residues from runoff. Corn is also grown in many coastal counties. Off-site movement of chemicals applied to cornfields in these counties may enter estuarine areas which support important marine fishery resources and wildlife communities.

Target Organisms

The target organisms for corn uses of fipronil include northern corn rootworm larvae, southern corn rootworm larvae, Mexican rootworm larvae, wireworms, seedcorn maggots, seedcorn beetles, billbugs, chinch bugs, grubs, and thrips.

Formulation Information

REGENT 1.5G is a granular dispersible formulation, applied by either *T-Band or In-Furrow application methods.

*Active Ingredient:
5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((1,R,S)-(trifluoromethyl)sulfinyl)-1-H-pyrazole-3-carbonitrile..1.5%
Inert Ingredients...98.5%

* The registrant has volunteered to delete T-Band application methods from this proposed 1.5G use on corn in order to further mitigate risks to avian species.

REGENT 80 WG is a dry powder flowable water dispersable formulation, applied by either foliar spray * or ground spray methods depending on the crop use.

**Active Ingredient:
Fipronil...80%
Inert Ingredients.............................20%
*- Foliar spray does not pertain to corn use.
**Contains 0.833 pounds of active ingredient per pound of product.

REGENT 3 G, [redacted] granular product for at plant in-furrow application to field corn. The label instructs that all granules, including those at the ends of turn rows, should be lightly incorporated.

Active Ingredient: Fipronil..........................3%
Inert Ingredients.......................................97%

Regent 4SC is a flowable concentrate. It is applied into the furrow as a solid stream after dissolving in water or liquid fertilizer.

Active Ingredient: Fipronil............................40%
Inert Ingredients...60%

Application Methods, Directions, and Rates

Application Timing
80 WG: Make one in furrow application at planting time only.

1.5G: A single application is made at planting only.

3G: A single application made at planting only.

4SC: One in furrow application at planting only.
(More detailed information regarding label instructions is included as an addendum to this review)

Environmental Hazard Statements(excerpted from labels)

Regent 1.5G
This pesticide is toxic to aquatic and estuarine organisms (fish and invertebrates). Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Cover, incorporate or clean up granules that are spilled during loading or visible on soil surface in turn areas. Do not contaminate water when disposing of equipment wash water.

REGENT 80WG and REGENT 4 SC Labels
For terrestrial use. This pesticide is toxic to birds and aquatic and estuarine organisms (fish and invertebrates). Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water when disposing of equipment wash water.

REGENT 80 WG Label Only
This pesticide is highly toxic to bees exposed to direct treatment or residues on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area.

REGENT 3G
For terrestrial use. This pesticide is toxic to birds and aquatic and estuarine organisms (fish and invertebrates). Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Cover, incorporate, or clean up granules that are spilled during the loading or are visible on the soil surface in turn

areas. Do not contaminate water by cleaning equipment or disposal of wastes. Do not contaminate water when disposing of equipment washwaters.

B. Exposure Characterization

ENVIRONMENTAL FATE ASSESSMENT

Environmental Fate Summary

Based on supplemental and acceptable data, fipronil dissipation appears to be dependent on photodegradation in water, microbially mediated degradation, and soil binding. Data indicate that fipronil is relatively persistent and immobile in terrestrial environments. In aquatic environments, a determination of the environmental behavior of fipronil is more tentative because soil and aquatic metabolism studies provide contradictory data on fipronil persistence to microbially mediated degradative processes. Photolysis is expected to be major factor in controlling fipronil dissipation in aquatic environments. Fipronil degrades to form persistent and immobile degradates. Since fipronil and its degradates have a moderate to high sorption affinity to soil, it is likely soil sorption will control fipronil residue movement into ground and surface waters. Fipronil and its degradates, however, can have the potential to move in very vulnerable soils (*e.g.*, coarse-textured soils with low organic matter content). Fipronil is expected to move (primarily in dissolved state) with runoff water into surface waters. In-furrow fipronil applicationa are expected to limit runoff potential.

Environmental Fate Assessment

Fipronil is stable ($t_{1/2} > 30$ days) in pH 5 and pH 7 buffer solution and hydrolyzes slowly ($t_{1/2}$=28 days) in pH 9 buffer solution. The major hydrolysis degradate is RPA 200766 (5-amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoro-methanesulfinyl pyrazole. Photodegradation of fipronil is a major route of degradation (photodegradation in water half-life=3.63 hours) in aquatic environment. In contrast, fipronil photodegradation on soil surfaces (dark control corrected half-life=149 days) does not appear to a major degradation pathway. Major photolysis products of fipronil are MB 46513 (5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-4-trifluoro-methylpyrazole 350, and RPA 104615 (5-amino-3-cyano-1-(2,6-dichloro-4-trifluoro methyl phenyl) pyrazole-4-sulfonic acid). The chemical degradation of fipronil appears to be dependent predominately on photodegradation in water and, to a lesser extent, on alkaline-catalyzed hydrolysis

Fipronil degradation in terrestrial and aquatic systems appears to be controlled by slow microbially-mediated processes. In aerobic mineral soil, fipronil is moderately persistent to persistent ($t_{1/2}$= 128 to 300 days). Major aerobic soil degradates (>10% of applied of fipronil) are RPA 200766 and MB 46136 (5-amino-1-(2,6-dichloro-4-trifluoro methylphenyl)-3-cyano-4-trifluoromethyl-sulphonyl-pyrazole). Minor degradates (<10% of applied fipronil) are MB 45950 (5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-cyano-4-trifluoro-methyl-thio-pyrazole)and MB46513. Fipronil also is moderately persistent (anaerobic aquatic $t_{1/2}$ = 116-130 days) in anoxic aquatic environments. Major anaerobic aquatic degradates are MB 45950 and RPA 200766. Supplemental aerobic aquatic metabolism data indicate that fipronil degradation ($t_{1/2}$=14 days) is rapid in aquatic environments with stratified redox potentials. These data contradict the longer fipronil persistence reported in anaerobic aquatic and aerobic soil environments.

Fipronil has a moderate sorption affinity (K_f=4.19 to 20.69 mL/g; 1/n= 0.938 to 0.969; K_{oc}= 427 to 1248 mL/g) on five non-United States soils. Fipronil sorption appears to be lower (K_f< 5 mL/g) on coarse-textured soils with low organic matter contents. Desorption coefficients for fipronil ranged from 7.25 to 21.51 mL/g. These data suggest that fipronil sorption on soil is not a completely reversible process. Since the fipronil sorption affinity correlates with soil organic matter content, fipronil mobility may be adequately described using a K_{oc} partitioning model. Soil column leaching studies confirm the immobility of fipronil.

Conclusions regarding the environmental fate of fipronil degradates, except MB 46513, are more tentative because they are based on a preliminary review of interim data not a formal evaluation of a fully documents study report. Since discernable decline patterns for the fipronil degradates were not observed in metabolism studies, the degradates are assumed to be persistent ($t_{1/2}\approx$700 days) to microbially mediated degradation in terrestrial and aquatic environments. However, the fipronil degradate, MB46136, rapidly photodegrades ($t_{1/2}$=7 days) in water. Radiolabelled MB 46513, applied at 0.1 µg/g, had an extrapolated half-life of 630 or 693 days in loamy sand soils when incubated aerobically in the dark at 25°C. The major metabolite of MB 46513 was RPA 105048 (5-amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonyl pyrazone).

Fipronil degradates have relatively low potential mobility because of a moderate to high sorption affinity to soil. Organic carbon partitioning coefficients for fipronil degradates can range from 1150 to 1498 mL/g for MB 46513, 1619 to 3521 mL/g for MB 45950, and 1448 to 6745 mL/g for MB 46136. The high sorption affinity of fipronil degradates is expected to limit movement into ground and surface water.

Terrestrial field studies confirm observations of the relative persistence and immobility of fipronil residues in laboratory studies. Fipronil, formulated as a 1% granular, had half-lives of 1.1 to 1.5 months on bare ground in North Carolina (NC) and Florida (FL), 0.4 to 0.5 months on turf in NC and FL, and 3.4 to 7.3 months for in-furrow applications on field corn in California (CA), Nebraska (NE), NC, and Washington (WA). The fipronil degradates MB 46136, MB45950, and RPA 200766 were detected in the field studies. Fipronil residues were predominately detected in the 0 to 15 cm soil depth at all test sites. However, there was detection of fipronil, MB 45950, MB 46136 and RPA 200766 at a depth of 15 to 45 cm for in-furrow treatments on coarse sandy loam soil in Ephrata, Washington. Although the field dissipation half-life of individual residues was not reported, the half-life of combined fipronil residues (including fipronil, MB 46136, MB 46513, MB 45950, and RPA 200766) ranged from 9 to 16 months.

The bioconcentration factor for radiolabelled fipronil was 321X in whole fish, 164X in edible tissues, and 575X in non-edible tissues. Accumulated fipronil residues were eliminated (>96%) after a 14-day depuration period.

DEGRADATION

Hydrolysis (161-1)
MRID No. 42194701

Radiolabelled fipronil was stable (<3% degraded by day 30 posttreatment) in pH 5 and pH 7 buffered solutions and hydrolyzed slowly ($t_{1/2}$=28 days) in pH 9 buffer solutions. The major degradate of fipronil was RPA 200766. In pH 9 buffer solution, RPA 200766 reached a maximum concentration of 51.7% of applied radioactivity at 30 days posttreatment. These data suggest that abiotic hydrolysis of fipronil is an alkaline-catalyzed degradation process.

The study (MRID 42194701) fulfills the hydrolysis (161-1) data requirement for fipronil. No additional data are needed at this time.

Photodegradation in water (161-2)
MRID No. 42918661
Ref.#ID: ACD/EAS/Im/255 (Interim Study)

Radiolabelled fipronil had a half-life of 3.63 hours in pH 5 buffer solution when irradiated with Xenon light. There was no fipronil degradation in the dark controls. Two degradates, MB46513 and RPA 104615, were identified in irradiated test samples. MB 46513 reached a maximum concentration of ≈43% of applied radioactivity at 6 hours postexposure. RPA 104615 reached a maximum concentration of ≈8% of applied radioactivity. One unidentified degradate, characterized as with a molecular weight of 410 a.m.u., reached a maximum concentration of ≈5.5% of applied radioactivity. Radioactive volatiles were not detected (<0.04% of applied radioactivity) in ethylene glycol and NaOH gas traps.

The registrant submitted interim photolysis data (Ref.#ID: ACD/EAS/Im/255) on MB 46136. Preliminary review <u>suggest</u> the interim data <u>should</u> fulfill data gaps in the comprehensive environmental fate assessment for fipronil. EFED, however, reserves final judgment on data acceptance pending review of a complete data submission.

The study (MRID 42918661) fulfills the photodegradation in water data requirement (161-2). No additional data are needed at this time.

Photodegradation on soil (161-3)
MRID No. 42918662

Radiolabelled fipronil had a half-life of 34 days (dark control corrected half-life = 110 days) on loam soil when exposed to intermittent (8 hour photodegradation period) Xenon light. Radiolabelled fipronil had a half-life of 49 days in dark controls. Photodegradates were RPA 200766 (11% of applied), MB 46136 (4% of applied), MB 45590 (1.91% of applied), MB 46513 and RPA 104615 (each at 8% of applied). Organic volatiles were not detected (<0.5% of applied) in the gas traps from irradiated or dark control samples. However, carbon dioxide evolution was detected (2.5% of applied) from irradiated samples.

The study (MRID 42918662) fulfills the photodegradation on soil data requirement (161-3) for fipronil. No additional data are needed
at this time.

METABOLISM

Aerobic soil metabolism
MRID No. 42928663
MRID No. 44262830

Radiolabelled fipronil, applied at 0.2 µg/g, had half-lives ranging from 128 to 308 days in sandy loam and sand soils when incubated aerobically in the dark at 25°C. Major degradates of fipronil were identified as RPA 200766 (27 to 38% of applied) and MB 46136 (14-24% of applied). Minor degradates of fipronil were identified as MB 45950 (< 5%), MB 46513 (1% of applied), and MB 45897 (<1% of applied). Additionally, six unidentified degradates were detected (each < 4% of applied radioactivity) in sandy loam and sand soil samples. No discernable decline patterns were observed for the fipronil degradates during the testing period. Unextractable radioactivity accounted for 6 to 15% of the applied radioactive fipronil. Radioactive volatiles (organic + CO_2) did not account for a discernible amount of applied radioactivity.

Radiolabelled MB 46513, applied at 0.1 µg/g, had an extrapolated half-life of 630 and 693 days in loamy sand soils when incubated aerobically in the dark at 25°C. Major metabolites were RPA 105048 (5-amino-3-carbamoyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylsulfonyl pyrazone). RPA 105048 reached a reported maximum concentration of 0.014 ppm and 0.017 (14% and 17% of applied, respectively). In addition, an unidentified degradate was detected at a maximum concentration of 0.003 ppm or 3% of applied radioactivity. Radiolabelled volatiles (organic + CO_2) were also detected (≤2% of applied radioactivity).

The registrant submitted aerobic soil metabolism data for MB 46513. Since no aerobic soil metabolism data are available for the other fipronil degradates, it is assumed the fipronil degradates are persistent ($t_{1/2}$=700 days; stable) in terrestrial environments.

The study (MRID 42928663) in conjunction with the degradate metabolism study (MRID 44262830) fulfills the aerobic soil metabolism (162-1) data requirement for parent fipronil and MB46513. No additional data are needed at this time. EFED notes the registrant assumes that fipronil degradates MB45950 and MB46136 are persistent in terrestrial environments. Further refinement of the comprehensive fate and exposure assessment for fipronil would additional data on aerobic soil metabolism of MB45950 and MB46136.

Anaerobic Aquatic Metabolism (162-3)
MRID No. 43291704

Radiolabelled fipronil, applied at 0.75 ppm in water or 1.5 ppm in soil, had half-lives of 116-130 days in anaerobic pond water/sediment when incubated under N_2 in the dark. Major degradates of fipronil were MB 45950 (47% of applied) and RPA 200766 (18% of applied). MB 45950 was predominantly detected in the soil extracts. In contrast, RPA 200766 was detected in both water and soil extracts. Numerous minor degradates (≤6% of the applied radioactivity) were detected in soil and water extracts. Unextractable radioactivity accounted for ≈18% of the applied radioactive fipronil.

The study (MRID No. 43291704) fulfills the anaerobic aquatic metabolism (162-3) and anaerobic soil (162-2) data requirement for fipronil. No additional data are needed at this time.

Aerobic Aquatic Metabolism (162-4)
MRID No. 44261909

Radiolabelled fipronil, applied at 0.05 ppm (w/w), rapidly degraded ($t_{1/2} \approx 14.5$ days) in sandy loam soil when incubated under stratified redox conditions in the dark at 25°C. Parent fipronil had a maximum concentration of 0.0497 ppm (0.05 ppm application rate) at time 0 (immediately posttreatment), 0.0009 ppm at 90 days posttreatment, and < 0.0003 ppm at 365 days posttreatment. Major metabolites of fipronil were MB 45950 (82.58% of applied at 365 days posttreatment) and RPA 200766 (11.09% of applied at 60 days). Minor metabolites were RPA 105048 (7.73% of applied) and MB 46513 (0.33% of applied). Two unidentified metabolites had maximum concentrations ranging from 3.34 to 4.58% Organic volatiles had a maximum cumulative concentration of 0.0005 ppm. Radioactive CO_2 had a maximum cumulative concentration of 0.001 ppm (% of applied).

The study (MRID 44261909) provides supplemental data on aerobic aquatic metabolism of fipronil. The data are deemed supplemental because the aerobic aquatic metabolism data contradict the degree of fipronil persistence observed in anaerobic aquatic and aerobic soil laboratory studies. The registrant should provide a complete explanation for the rapid degradation half-life ($t_{1/2}$=14 days) of fipronil under the experimental conditions. The aerobic aquatic metabolism (162-4) data requirement is not fulfilled at this time. Additional data are needed to address disparate results in the reported metabolism studies.

Additionally, the registrant assumes that fipronil degradates MB46136, MB46513, and MB45950 are stable in aerobic aquatic environments. Further refinement of the comprehensive fate and exposure assessment for fipronil would require additional data on aerobic aquatic metabolism of MB45950, MB46136, and MB45950.

MOBILITY

Leaching mobility study (163-1)
MRID No. 42918664
MRID No. 43018801 and 44039003

Radiolabelled fipronil had Freundlich coefficients of 4.19 mL/g (1/n=0.947; K_{oc}= 1248) for sand loam soil, 9.32 mL/g (1/n=0.969; K_{oc}= 800) sandy clay loam soil, 10.73 mL/g (1/n=0.949; K_{oc}=673) for Speyer 2.2 soil, 14.32 mL/g (1/n=0.947; K_{oc}=427) for sandy clay loam soil, and 20.69 mL/g (1/n= 0.969; Koc=486)for loam soil. Desorption coefficients for fipronil ranged from 7.25 to 21.51 mL/g. Fipronil sorption appears to be lower (K_f< 5 mL/g) on coarse-textured soils with low organic matter contents. These data suggest that fipronil sorption on soil is not a completely reversible process. Since the fipronil sorption affinity correlates (r= 0.97) with soil organic matter content, fipronil mobility may be adequately described using a K_{oc} partitioning model. Soil column leaching studies confirm the potential immobility of fipronil.

Radiolabelled fipronil was relatively immobile (>80% of the applied radioactivity in the 0-to-8 cm segment) in soil columns for five different foreign soils including a German loamy soil, Manningtree UK loamy sand (called sandy loam in study), Manningtree UK loam, French sandy clay loam (1), and French sandy clay loam (2). In the Manningtree UK loamy-sand soil, however, radiolabelled fipronil residues were detected in the 0-14 cm segment. Radioactive fipronil residues (1-8% of applied) were detected in leachate samples from all test soils. Leachate residues were not identified.

Radiolabelled MB 46513 had Freundlich adsorption coefficients of 4.3 mL/g (K_{oc}=1150 mL/g) for sand soil, 5.1 mL/g (K_{oc}= 1498 mL/g) for loamy sand soil, 5.5 mL/g (K_{oc}=1164 mL/g) for silt loam soil, 15.2 mL/g (K_{oc}=1245 mL/g) for clay, and 69.3 mL/g for pond sediment (K_{oc}=1392). Initial desorption coefficients of MB46513 are 5.8, 5.9, 6.2, 14.7, and 66.2 mL/g for sand, loamy sand, silt loam, clay, and pond sediment, respectively. All soils and sediment showed increasing K_{des} values (cycle 2 K_{des} values ranged from 6.9 to 73.6 mL/g and cycle 3 K_{des} values ranged from 9.5 to 85.9 mL/g) for successive desorption cycles. These data suggest that MB 45950 sorption on soil is not a completely reversible process.

The degradates MB 45950 and MB 46136 have a moderate to high sorption affinity to organic carbon. Interim data indicate MB46136 had K_{oc} adsorption coefficients of 5310 mL/g in a silt loam soil, 4054 mL/g in a sandy loam soil, 6745 mL/g in a loam soil, 3486 mL/g in a sandy clay loam soil, and 1448 mL/g in silt loam soil. MB 45950 had K_{oc} adsorption coefficients of 2404 mL/g in a silt loam soil, 3120 mL/g in a sandy loam soil, 2925 mL/g in a loam soil, 3521 mL/g in a sandy clay loam soil, and 1619 mL/g in silt loam soil.

Aged soil column leaching studies demonstrated immobility of RPA 200766, MB 45950, MB 46136 and RPA 104615. RPA 200766 was detected (2-17% of applied) in all soil columns except the Manningtree sandy loam. Detections of MB 45950 and MB 46136 were more sporadic in soil columns. Radioactive residues were detected (< 1 to 4% of applied radioactivity) in leachate samples. Leachate residues were not identified.

The unaged residue mobility studies (MRID No.43018801 and 42918664) fulfill the batch equilibrium/adsorption-desorption data (163-1) requirement for fipronil. The aged residues mobility studies (MRID No. 43018801 and 42918664) in conjunction with batch equilibrium studies on MB 46513 (MRID 44262831), MB 46136 and MB 45950 (Theissen, 10/97) should fulfill the aged portion of the 163-1 data requirement. EFED notes the batch equilibrium data for MB 46136 and MB 45950 were taken from interim reports. Complete study submissions for the interim reports are needed to confirm the validity of the batch equilibrium data.

DISSIPATION

Terrestrial field dissipation (164-1):
MRID No. 43291705, 43401103, 44298001

Fipronil, applied as REGENT 1.5G at an in furrow rate of 0.13 lbs a.i./A, had dissipation half-lives ranging from 3.4 to 7.3 months in a loam soil in San Juan Bautista, CA, a clay loam soil in York, NE, a sand soil in Clayton, NC, and a loamy sand soil in Ephrate, WA. Degradation products of fipronil detected in field soils were MB 46136, MB 45950, and RPA 200766. Fipronil residues were detected predominately in the top 0 to 15 cm soil depth at all test sites. However, there was detection of fipronil, MB 45950, MB 46136 and RPA 200766 at a depth of 15 to 45 cm for in-furrow treatments on coarse sandy loam soil in Ephrata, Washington. Although the field dissipation half-life of individual residues was not reported, the half-live of combined fipronil residues (including fipronil, MB 46136, MB 46513, MB 45950, and RPA 200766) ranged from 9 to 16 months.

Fipronil, applied at a rate of 0.05 lbs a.i/A, had dissipation half-lives of 1.1 months for bare ground on sand soil in Florida, 0.4 months for turf on a sand soil in Florida , 1.5 months for bare ground on loamy sand soil in North Carolina, and 0.5 months for turf on sandy loam soil in North Carolina. MB 46136 and RPA 200766 were detected (>2 µg/kg) in field soil samples. MB 46136 had a maximum concentration ranging from 5.6 to 8.9 µg/kg at 2-3 months post treatment. RPA 200766 was detected in bare ground samples at a maximum concentration of 3.7 µg/kg at 3 months posttreatment. Despite excess rainfall/irrigation levels, the fipronil residues remained in the upper 6 inch soil layer at each location during the 4 month testing period. Although the field dissipation half-life of individual residues was not reported, the half-live of combined fipronil residues (including fipronil, MB 46136, MB 46513, MB 45950, and RPA 200766) ranged from 2.5 to 5.33 months. EFED notes there was generally a poor fit (R2=0.3 to 0.7) of the first-order degradation model to describe combined fipronil residue dissipation.

REBUTTAL: The registrant provided a rebuttal (MRID 44298001) to the EFED review of in furrow field dissipation of fipronil (MRID 43401103). EFED stated that "additional terrestrial field data may be needed for turf and spray applications > 0.05 lb a.i./A". The registrant stated that the Regent 80WG and Regent 1.5G formulations will have similar behavior because 1.) they are applied at the same rate, 2.) the environmental behavior of formulations should be similar because both formulations, applied either as clay suspension formulation or direct spray application on soil, will be controlled by sorption on soil or clay surfaces, and 3.) field dissipation studies for in-furrow Regent 1.5G use on corn (MRID 43401103) has similar rates and routes of dissipation of Regent 80WG (MRID 44262826, 44262827, 43401103, and 43291705) on turf, cotton, or potatoes. Therefore, the registrant asssessed that in-furrow field dissipation studies for REGENT 1.5 (MRID 43401103) are sufficient to demonstrate field dissipation behavior of fipronil from in-furrow use of REGENT 80 WG. EFED accepts the registrant rebuttal that field dissipation studies on in-furrow use REGENT 1.5G at 0.13 lbs a.i./A can support in furrow use of REGENT 80WG at 0.13 lbs a.i./A. Acceptance of the registrant's rebuttal is based on the fact the mode of application and application rates are similar for the REGENT 1.5G and REGENT 80WG. Additional field data may be needed to support new formulations, application methods, and application rates.

The studies MRID 43291705 and 43401103 in conjunction with the registrant's rebuttal (MRID 44298001) satisfy the terrestrial field dissipation (164-1) data requirement for in furrow use of fipronil on field corn. No additional data are needed to support in furrow fipronil uses on field corn at application rates < 0.13 lbs a.i/A.

ACCUMULATION

Fish Accumulation (165-4):
MRID No. 43291706, 43291707, 44298002

The bioconcentration factor (BCF) of radiolabelled fipronil, applied at a constant concentration of ≈900 ng equiv.L^{-1}, in bluegill sunfish was 321X in whole fish, 164X in edible tissue, and 575X in non-edible tissues. Major fipronil residues in fish tissues were identified as MB 46136, MB 45897, and MB 45950. In edible fish tissues, the maximum residue concentration was 55% of accumulated for MB 46136, 14% of accumulated for MB 45897, and 9% of accumulated for MB 45950. In inedible fish tissues, the maximum residue concentration was 59% of accumulated for MB 46136, 23% of accumulated for MB 45897, and 9% of accumulated for MB 45950. In whole fish tissues, the maximum residue concentration was 28% of accumulated for MB 46136, 24% of accumulated for MB 45897, and 9% of accumulated for MB 45950. RPA 200766 was as a minor degradate in fish tissues. Accumulated fipronil residues were eliminated (>96%) after a 14 day depuration period.

REBUTTAL: The registrant provided a rebuttal (MRID 44298002) to the EFED review of bioaccumulation in fish studies (MRID 43291706 and 43291707). EFED stated that "storage stability data for tissue samples and the length of storage of tissue samples were not reported. These data are needed to validate the tissue characterization data." The registrant stated that storage stability information were provided by chromatographic profiling of fipronil residues from stored tissue samples over a 4-5 month storage period. Chromatographic profiling showed that new GC retention peaks were not present over the 4 to 5 month storage period (Figures AII5, page 34-39). The registrant also stated the storage stability information of fipronil residues in fish tissues is sufficient to meet the Health Effects Division guidance on the conduct of storage stability studies. Additionally, the registrant stated that fipronil residues were shown to be stable for 2 years in animals tissues (MRID 43884008).

EFED accepts the registrant's rebuttal that sufficient information was submitted to illustrate stability of fipronil residues in fish tissues. EFED notes that storage stability samples should be prepared along with spiked samples at the initiation of laboratory studies and should be treated exactly like the test samples. The frequency of analysis depends on the stability of test residues, but should at a minimum be analyzed at the initiation and termination of the study. In future studies, storage stability studies should be performed in this manner.

The studies MRID 43291706 and 43291707 in conjunction with rebuttal comments, MRID 44298002, satisfy the bioaccumulation in fish (165-4) data requirement. No additional data are needed at this time.

Water Resource Assessment

Since fipronil is being registered for such a widely-grown crop as field corn, the water resource assessment will focus the major corn production regions. The geographic distribution of field corn is associated with the following major resource land areas (MRLAs): 1) Central Feed Grains and Livestock Region; 2) Atlantic and Gulf Coast Lowland Forest and Truck Crop Region; 3) Eastern Section of the South Atlantic and Gulf Slope Cash Crop, Forest, and Livestock Region; 4) Northern Atlantic Slope Truck, Fruit, and Poultry Region; 5) Lake States Fruit, Truck, 6) Western Great Plains and Irrigated Region; and 7) Northern Great Plains Spring Wheat and Dairy Region (Austin, 1972). These regions are predominately representative of the range climatic conditions found in the eastern two-thirds of the United States. The precipitation gradient can range from 50 inches in the Northern Atlantic Slope Truck, Fruit, and Poultry Region to 20 inches in the western section of Western Great Plains and Irrigated Region. Although the distribution of precipitation varies among the corn growing regions, it is generally highest from late spring to midsummer.

Further analysis of the corn production area indicates some localized regions have a high pesticide vulnerability index for contamination of shallow ground water because of the presence of Group A soils (Kellog et al., 1992). These regions are the coastal plains of Georgia, S. Carolina, and N. Carolina; the eastern section of Nebraska; the eastern shore region of Lake Ontario; and the Delmarva Peninsula area. Many of these areas (e.g., Delmarva Peninsula) border sensitive natural habitats. The majority of the corn growing area are classified as Hydrologic Group B soils. These soils are characterized by moderately high to high saturated hydraulic conductivities (K_{sat}=0.36 to 3.60 cm/hr) with deep to very deep ground water and are of limited concern for groundwater contamination. The major Group B soil subgroups are classified as Argiudolls, Hapludolls, Hapludalfs, Dystrochepts. Small areas of concentrated Group C soils are found in Ohio, southern Iowa and Illinois, and Eastern Indiana. The major Group C soil subgroups are Hapludults and Hapludalfs. Also, the Gulf coast region of Texas consist of high concentration of Group D soils. The major Group D soil subgroups are Ochraquults, Haplaquolls, Humaquepts, and Pelluderts. Group C and D soils are more prone to surface water runoff because of lower saturated hydraulic conductivities and/or relatively high water table.

SURFACE WATER ASSESSMENT

Based on the environmental fate assessment, fipronil and its degradates (MB 46513, MB 46136 and MB 45950) can potentially move into surface waters. Since fipronil is used as an in-furrow application on field corn, the runoff potential of fipronil residues is expected to be lower than for unincorporated surface application techniques. However, the persistence of parent fipronil ($t_{1/2}$=128 to 300 days) and its transformation products ($t_{1/2}$=700 days) may allow for a substantial fraction of fipronil residues to be available for runoff months after application. Fipronil and its transformation products have a moderate to high binding affinity (K_d values 4 to 20 mL/g) to mineral soils. Although fipronil and its degradates exhibit moderate soil sorption affinities, these compounds are expected to exist in runoff waters primarily in the dissolved state.

The dissipation of fipronil in surface water should be dependent on photodegradation in water ($t_{1/2}$ = 3.63 hours) and, to a lesser extent, microbial-mediated degradation ($t_{1/2}$ = 128 and 300 days for aerobic soil; 116 to 130 days for anaerobic aquatic; 14 days for aerobic aquatic metabolism). Since photodegradation is a major route of degradation for fipronil, its dissipation is expected to be dependent on physical components of the water (*i.e.* sediment loading) which affect sunlight penetration. For example, fipronil is expected to degrade faster in clear, shallow water bodies than in murky and/or deeper waters. Since fipronil and its transformation products have moderate soil-water partitioning coefficients, binding to sediments may also be a route of dissipation.

The following data were used as input for the GENEEC and PRZM/EXAMS modeling of fipronil:

Parameter	Value	Source
Soil K_{oc}	727 mL/g[1]	MRID 44039003
Aerobic soil half-life	128 days	MRID 42918663
Photolysis half-life	0.16 days	MRID 42918661
Hydrolysis pH 7	Stable	MRID 42194701
Aerobic Aquatic half-life	Stable[2]	
water solubility	2.4 mg/L	EFGWB one-liner

1- Mean Koc value.

2- Fipronil is considered to be stable in aerobic aquatic environments because the aerobic aquatic metabolism study (MRID 44261909) was deemed as supplemental data.

Based on the Tier 1 GENEEC surface water modeling, the maximum fipronil concentration in surface water is not likely to exceed 2 µg/L (Table 1). Tier II PRZM-EXAMS modeling indicates the 90[th] percentile maximum fipronil concentration in surface water is not likely to exceed 0.7 µg/L (Table 1;

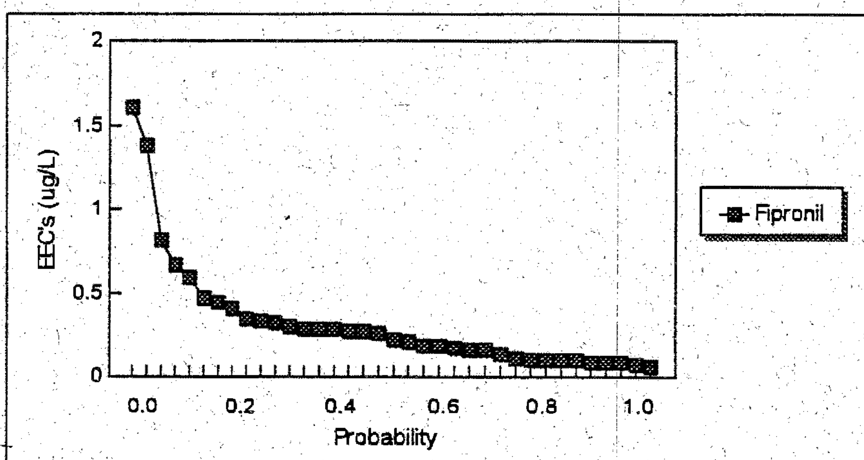
Figure 1). An earlier Tier II assessment on fipronil indicates the 90th percentile maximum concentration of fipronil is not likely to exceed 0.280 µg/L. Based on PRZM-EXAMS modeling, the acute and chronic drinking water concentration for fipronil is not likely to 0.715 and 0.276 µg/L, respectively. The Tier II assessment was conducted on a corn site in Yazoo County, Mississippi (MLRA-134). The soil on the site is classified as a Loring silt loam (fine-silty, mixed, Thermic Typic Fragiudalf). Please see attached PRZM-EXAM assessment. The Tier II assessments were conducted on a soil with a very dense "hard pan" horizon commonly known as a fragipan. A fragipan can encourage lateral flow of water because of water impedance through the soil profile. The soil hydrology effects associated with the presence of a fragipan were not considered in the modeling.

Table 1: Fipronil EECs from In-Furrow Use on Corn

Model	Peak EEC (PPB)	4-day EEC (PPB)	21-day EEC (PPB)	56-day EEC (PPB)	90-day EEC (PPB)
GENEEC(parent)	2.05	1.91	1.35	0.78	
PRZM/EXAMS*	0.715	0.649	0.500	0.276	0.276

*1 in 10 year EECs are reported.

Figure 1: Maximum PRZM/EXAMS EECs for Fipronil Use on Yazoo, MS Corn Site



EFED notes differences in K_{oc} input parameters for current modeling and earlier PRZM-EXAMS surface water modeling. Earlier Tier II assessment was conducted using a mean K_{oc} of 803 mL/g (Mostaghimi, 1996). Subsequent review of the available data suggest that this earlier K_{oc} was in error. The correct mean K_{oc} of fipronil is 727 mL/g. Although the surface water models are sensitive to K_{oc}, the slight difference in fipronil K_{oc} is expected to only slightly increase the estimated environmental concentrations. The mean K_{oc} was used because there was an observed correlation between K_d and soil organic matter.

The lowest reported half-life of fipronil ($t_{1/2}$= 128 days) was used as the representative aerobic soil metabolism half-life of fipronil. Preliminary analysis indicates the upper 90th percentile half-life value of the mean is much greater than the highest reported value ($t_{1/2}$= 308 days). The highest reported half-life is associated with a low organic matter sand, which likely represents a soil type of limited microbial activity and is not characteristic of corn growing regions. The lowest reported half-life is derived from a sandy loam soil, which is expected to be more representative of soil under corn production. It should be noted that the use of the lowest half-life is a departure from current EFED policy, which states that the 90th percentile of the mean should be used for modeling purposes. However, the use of the lower half-life is not expected to alter PRZM/EXAMS predictions because the model is relatively insensitive with respect to this parameter for moderately to persistent compounds.

The GENEEC and PRZM/EXAMS modeling assumes that fipronil is stable to aerobic aquatic metabolism. This assumption was used because the aerobic aquatic metabolism data for fipronil was deemed as supplemental. EFED notes that rapid degradation of fipronil ($t_{1/2}$=14 days) in the aerobic aquatic metabolism study is inconsistent with both aerobic soil metabolism and anaerobic aquatic metabolism data on fipronil. Additionally, interpretation of the study results are further confounded by a highly stratified redox potential between the water and sediment phases. Therefore, a conservative assumption of fipronil stability was used for GENEEC and PRZM-EXAMS modeling.

EFED conducted Tier 1 surface water modeling for the individual degradates including MB 46513, MB 46136 and MB45950. Environmental fate properties of the fipronil degradates are shown in Table 2. EFED notes the environmental fate data for MB 46136 and MB 45950 were taken from interim reports. Preliminary review of interim data suggest the interim data should be satisfactory to fulfill data gaps in the comprehensive environmental fate assessment. EFED, however, reserves final judgment on data acceptability pending review of final data submissions.

Table 2: Fate Properties of Fipronil Degradates

Fate Parameter	MB 46136	MB 46513	MB 45950
Mean Koc	4208 mL/g	1290 mL/g	2719 mL/g
Aerobic Soil Metabolism Half-life	Stable	Stable	Stable
Aqueous Photolysis Half-life	7 days	Stable	Stable
Hydrolysis Half-life	Stable	Stable	Stable
Aerobic Aquatic Metabolism Half-life	Stable	Stable	Stable
Water Solubility	0.16 mg/L	0.95 mg/L	0.1 mg/L
Application Rate* (lbs a.i./A)	0.039	0.0013	0.0065
References	**RP# 201555 ACD/EAS/Im/255 Theissen 10/97**	MRID 44262831 44262830 **Theissen 10/97**	**RP 201578 Theissen 10/97**

*based on percent of degradate formation in aerobic soil metabolism studies

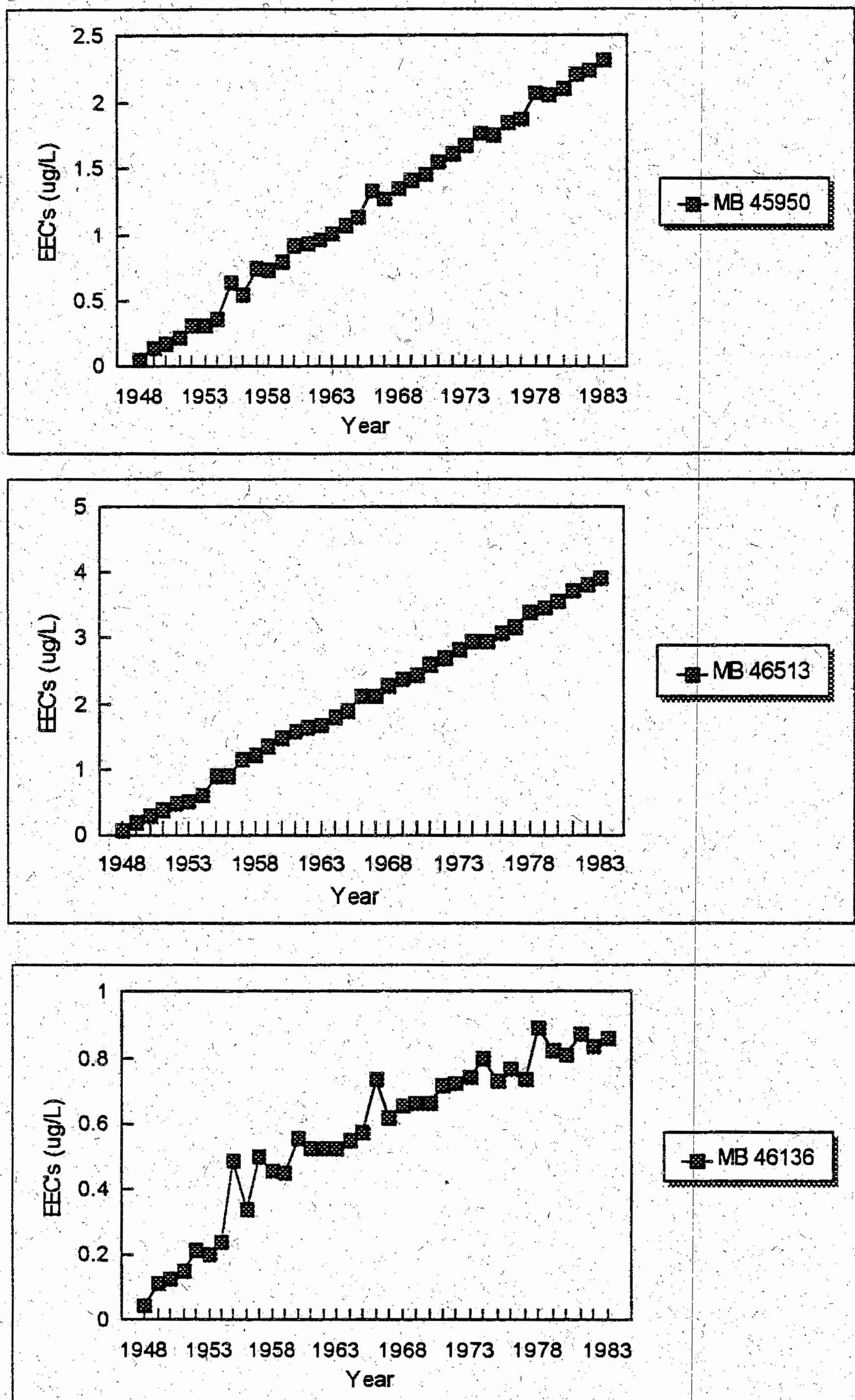
Based on the Tier 1 GENEEC surface water modeling, the maximum concentration of fipronil residues in surface water is not likely to exceed 0.168 µg/L for MB 46136, 0.014 µg/L for MB 46513, and 0.039 µg/L for MB 45950 (Table 3). The EECs for the individual fipronil degradates are highly dependent on the application rate. Since the individual fipronil transformation products represent only a fraction of the applied fipronil, the application rates of the fipronil degradates are representative of maximum percentage of degradate formation in aerobic soil metabolism studies. EFED notes that MB 46513 and MB 45950 are not major aerobic soil degradates of fipronil. A major photodegradate of fipronil, MB 46513, is not expected to be major degradate for in-furrow applications of fipronil. The degradate MB 45950 appears to be formed in anoxic to suboxic environments. These conditions are not likely to be representative of most surface soils.

Table 3: Fipronil Degradate GENEEC EECs for In Furrow Use on Corn

Degradate	Peak EEC (µg/L)	4-day EEC (µg/L)	21-day EEC (µg/L)	56-day EEC (µg/L)
MB 46136	0.168	0.152	0.100	0.062
MB 46513	0.014	0.013	0.011	0.009
MB 45950	0.039	0.036	0.027	0.019

Tier II PRZM-EXAMS modeling for individual fipronil degradates indicates that they are persistent enough to accumulate in surface water bodies (Figure 2). Fipronil degradate concentrations from a 36-year PRZM-EXAMS simulation can accumulate potentially from 0.005 to 3.9 µg/L for MB 46513, 0.004 to 2.3 µg/L for MB45950, and 0.004 to 0.89 µg/L MB46136. Probabilistic assessment of the fipronil EECs is not possible because accumulation of residues indicate temporal dependence (correlation) between successive years. EFED notes, however, the Tier II assessment assumes long-term use of fipronil in an isolated farm pond watershed. This scenario is expected to be highly conservative because the "farm-pond" runoff scenario does not account for dilution.

Figure 2. Maximum PRZM-EXAMS EEC's for Fipronil Degradates



Uncertainties in the surface water assessment include: 1.) the actual degradation rate of fipronil in aquatic environments and 2.) the limited environmental fate data for fipronil degradates. The lack of acceptable aerobic aquatic metabolism data prevents a complete assessment of fipronil degradation in aquatic environments. Contradiction of fipronil half-lives among the various metabolism studies needs to be addressed by the registrant. The lack of metabolism half-lives for fipronil degradates also limits confidence in prediction of environmental concentrations. The absence of or low confidence in the metabolism data dictated the conservative assumption that degradates are "stable" in aquatic and terrestrial environments. Such an assumption suggests that fipronil residues could potentially accumulate in terrestrial or aquatic environments.

GROUND WATER ASSESSMENT

The environmental fate data for fipronil indicate a moderate to high persistence and relatively low mobility in terrestrial environments. Based on the SCI-GRO model, acute drinking water concentrations in shallow ground water on highly vulnerable sites are not likely to exceed 0.055 µg/L for parent fipronil, 0.001 µg/L for MB 46136, 0.00026 µg/L for MB 46513, and 0.00036 µg/L for MB 45950. Chronic concentrations are not expected to be higher than acute values. Highly vulnerable sites are those with low organic matter, coarse textured soils (e.g., sands and loamy sands) and shallow ground water. The fate data for fipronil and its degradates indicate a higher potential mobility on coarse-textured soils (sand or loamy sands). Such soils in the corn growing region are located predominately in the coastal plains of Georgia, South Carolina, and North Carolina; eastern section of Nebraska; the eastern shore region of Lake Ontario; and the Delmarva Peninsula (Kellog et al., 1992). Fipronil and its degradates may pose a threat to ground water contamination within these sensitive areas.

Estimated Terrestrial Environmental Concentrations and Their Duration:

Exposures for terrestrial organisms are estimated using two approaches. The first approach, applicable to granular formulation applications involves calculation of granules and associated mass of active ingredient concentrations at the soil surface. The second approach, applicable to in-furrow spray applications, involves calculation of soil concentrations of fipronil and degradates and subsequent concentrations in selected dietary components of terrestrial receptors.

Granular Formulation Terrestrial Exposure Estimates

The labels for 1.5 G and 3G formulations of fipronil permit T-band applications in 7 inch bands. It is important to note the registrant agreed to delete T-band use for the 1.5G and 3G formulations. It is anticipated that adequate incorporation of granules will limit ingestion of most granules by birds foraging in soil. The Agency assumes that 1% and 8% granular exposure can occur from in furrow and T-band applications, respectively. This assumption would correspond to 0.41 mg a.i./ft^2 for in-furrow and 0.47 mg a.i./ft^2 for T-band applications.

In-Furrow Spray Terrestrial Exposure Estimates

Although the standard terrestrial exposure assessment assumes foliar deposition on different non-target crops, it may not be completely applicable because fipronil use on corn is strictly limited to in-furrow application. This type of application is expected to cause direct deposition on soil and limit direct foliar deposition. The maximum soil concentrations of fipronil from a single in furrow application could range from 33.94 ppm (ca. 1 cm depth) to 2.26 ppm (ca. 15 cm depth). This concentration range accounts for application efficiency from the in furrow application process. These estimates are applicable only to soil particles and potential food sources in or surrounding furrows where ground sprays are applied. As nozzles will concentrate residues in small bands within the application site, residues on soil are expected to be limited to the immediate target zone of the spray.

Table 4 summarizes the estimated immediate posttreatment soil concentrations of fipronil and fipronil degradates (MB45950 and MB46136) as a result of in-furrow application.

Table 4. Estimated Soil Concentrations for Fipronil and Degradates In-Furrow Application (Immediately Posttreatment)

Chemical	Soil Concentration (mg/kg) ca 1 cm	Soil Concentration (mg/kg) ca 15 cm
fipronil	33.94	2.26
MB45950	1.69*	0.12
MB46136	8.14**	0.54

* assumes a 5% conversion efficiency

** assumes a 24% conversion efficiency

In-furrow spray application of fipronil to corn field soils is an application scenario not normally covered by routine exposure/risk assessment methods employed by EFED. Such a spray application does not involve application of active ingredient as a granule, precluding the use of the granular pesticide assessment methodology. Similarly, the extremely limited zone of spray application, restricted to individual furrows, would not involve general application across a field with concomitant residues on bare ground, foliage, etc. This would suggest that the use of Fletcher (1994) spray application residue values would not be reflective of such sprays applied to soil within individual furrows. Because the in furrow spray application is not compatible with these routine methods of risk assessment for terrestrial receptors, EFED utilized a new approach for evaluating the exposure to terrestrial birds and mammals potentially foraging in corn fields treated with fipronil by this in furrow spray method.

EFED has considered a variety of potential terrestrial receptors associated with corn fields. In selecting receptor organisms EFED has focused on species with a potential for feeding in corn fields and organisms with a comparatively wide geographical distribution that would afford a reasonable approximation of potential risks across the wide areas of potential fipronil use on corn. Terrestrial wildlife foraging in or near application furrows may be exposed to residues adsorbed to soil particles or accumulated in soil organisms. Under the in-furrow spray scenario, exposures to wildlife were calculated as an oral dose (average mg/kg-bw./day). The assessment of risk was based on comparison to oral toxicity thresholds for the most sensitive species tested. Three species were selected as terrestrial receptors: bobwhite quail, American robin, and meadow vole.

Pastorok et al. (1996) has summarized a basic chemical intake model for wildlife species to average daily dietary exposure dose for a given chemical of concern and a given receptor species. The general structure of this basic chemical intake model is as follows:

$$IR_{chemical} = \left[\sum (C_i)(M_i)(A_i)/W\right]$$

where: $IR_{chemical}$ is the species-specific total rate of intake of chemical by ingestion (mg/kg-bw/day)

C_i is the chemical concentration in medium I (mg/kg) (e.g., soil, water, and dietary components)

M_i is the rate of ingestion of medium I (kg/day)

Ai is the gastrointestinal absorption efficiency of the chemical in medium I relative to absorption in laboratory toxicity tests

W is the body weight of the receptor species (kg)

This basic model was used to estimate oral dose exposures for the three receptor species selected for risk assessment. Because of a lack of data regarding absorption efficiencies both in the available toxicity studies and for free-living receptors, the absorption efficiency (A_i) for all three receptor species was conservatively assumed to be 100% or 1.0.

The model used for estimating oral dose exposure for the robin was based on a simple two-component model that considered incidental ingestion of soil and consumption of soil invertebrates (i.e., earthworms). The equation describing this model is as follows

$$\text{robin exposure in mg/kg-bw/day} = \frac{((C_{worm}\ \text{mg/kg})(0.15)(0.0082\ \text{kg food/day}) + (C_{ss}\ \text{mg/kg})(0.00082\ \text{g soil/day})}{0.081\ \text{kg body weight}}$$

where: C_{worm} is the estimated concentration in earthworms as calculated by fugacity relationships and the predicted concentration of chemical over a 15 cm soil profile (see explanation below)

0.15 is the fraction of robin diet attributable to earthworms (EPA 1993)

0.0082 kg food/day is the food ingestion rate for adult robins as calculated using allometric relationships from Nagy (1984)

C_{ss} is the predicted concentration of chemical in the upper 1 cm of soil. The chemical over the 1cm soil depth was selected as the reasonable depth-integrated concentration available for incidental soil ingestion

0.00082 kg soil/day is calculated from the fraction of diet (0.1) that consists of incidentally ingested soil as per data for soil invertebrate feeding birds (Beyer et al. 1994, EPA 1993) and the estimated daily dietary intake as per Nagy (1987)

0.081 kg body weight is the average body weight of adult robins for data reported in EPA (1993)

The model for estimating oral exposure for the bobwhite considered incidental soil exposure only. Data available in EPA (1993) suggest that bobwhite quail are not routine consumers of earthworms, hence the limitation of the exposure model to incidental soil ingestion only. The model is as follows

$$\text{quail exposure in mg/kg-bw/day} = \frac{(C_{ss}\ \text{mg/Kg})(0.00139\ \text{kg soil/day})}{0.178\ \text{kg body weight}}$$

where: C_{ss} is the predicted concentration of chemical in the upper 1 cm of soil. The fipronil over the 1cm soil depth was selected as the reasonable depth-integrated concentration available for incidental soil ingestion

0.00139 kg soil/day is an assumed fraction of diet that consists of incidentally ingested soil as per data for gallinaceous birds 0.094 of daily diet mass (Beyer et al. 1994, EPA 1993) and a calculated dietary intake of 14.74 g as per Nagy (1987)

0.178 kg body weight is the average body weight of adult quail for data reported in Dunning (1984)

The meadow vole exposure model considers incidental ingestion of soil only. Available data in EPA (1993) suggest that meadow voles do not routinely consume earthworms. The exposure model is as follows:

$$\text{meadow vole exposure in mg/kg-bw/day} = \frac{(C_{ss}\ \text{mg/Kg})(.00035\ \text{kg soil/day})}{0.043\ \text{kg body weight}}$$

where: C_{ss} is the predicted concentration of chemical in the upper 1 cm of soil. The fipronil over the 1cm soil depth was selected as the reasonable depth-integrated concentration available for incidental soil ingestion

0.00031 kg soil/day is an assumed fraction of diet that consists of incidentally ingested soil as per data for meadow voles 0.024 of daily diet mass (Beyer et al. 1994, EPA 1993) and a calculated dietary intake of 13.05 g as per EPA (1993)

0.043 kg body weight is the average body weight of adult meadow voles EPA (1993)

An estimation of fipronil and its degradate concentrations potentially accumulated in the tissues of earthworms was required to complete the exposure estimates for robins. This estimation of earthworm concentration was calculated using a fugacity-based (equilibrium partitioning) approach based on the work of Trapp and McFarlane (1995) and Mackay and Paterson (1981). Earthworms dwelling within the soil are exposed to contaminants in both soil pore water and via the ingestion of soil (Belfroid et al. 1994). The concentrations of fipronil and its degradates in earthworms were calculated as a combination of uptake from soil pore water and gastrointestinal absorption from ingested soil:

$$C_{earthworm} = [(C_{soil})(Z_{earthworm}/Z_{soil})]+[(C_{soil\ water})(Z_{earthworm}/Z_{water})]$$

where:

C_{soil} is the concentration of chemical in bulk soil (note: a chemical concentration averaged over a 15 cm soil depth was used to reflect a concentration across the earthworm occupied area of soil)

$Z_{earthworm}$ is the fugacity capacity of chemical in earthworms = $(lipid)(K_{ow})(\rho_{earthworm})/H$

Z_{soil} is the fugacity capacity of chemical in soil = $(K_d)(\rho_{soil})/H$

Z_{water} is the fugacity capacity of chemical in water = $1/H$

$C_{soil\ water}$ is the concentration of chemical in soil water = C_{soil}/K_{bw}

K_{bw} is the bulk soil-to-water partitioning coefficient = $(\rho_{soil})(K_d)+\theta+(\epsilon-\theta)(K_{aw})$

K_{aw} is the air-to-water partitioning coefficient = H/RT

H = Henry's Constant specific to fipronil or degradate

R = universal gas constant, 8.31 Joules-m^3/mol-°K

T = temperature °K, assumed to be 298 °K

K_d = soil partitioning coefficient = (chemical K_{oc})(0.02 assumed fraction of soil organic carbon)

ρ_{soil} = bulk density of soil, assumed to be 1.3 g/cm^3

θ = volumetric fraction of the soil, assumed to be 0.30

ϵ = volumetric total porosity of the soil, assumed to be 0.50

lipid = fraction of lipid in organism 0.01 (Cobb et al. 1995)

K_{ow} = fipronil or degradate octanol to water partitioning coefficient

$\rho_{earthworm}$ = the density of the organism g/cm^3, assumed to be 1 g/cm^3

Table 5 summarizes the model inputs and exposure estimates for robins, bobwhite quail, and meadow voles.

Table 5. Model Input Parameters and Dietary Exposure Estimates for Avian and Mammalian Receptors (for Soil Concentrations Immediately Posttreatment)

Parameter	Fipronil	MB45950	MB46136
C_{soil} (mg/kg @ 15 cm depth)*	2.26	0.124	0.54
C_{ss} (mg/kg @ 1 cm depth)	33.94	1.69	8.14
Henry's Constant (Pa-m³/mole)	4.406E-01	6.37E-03	1.315E-01
R universal gas constant (Joules-m³/mol-°K)	8.314	8.314	8.314
T °K	298	298	298
K_{ow}	10570	6310	2818
K_d (L/kg)	14.54	84.12	54.36
Z_{water} (1/H or moles/Pa-m³)	2.269632	156.9859	7.604563
Z_{soil} (($K_d \cdot \rho_{soil}$)/H)	42.90059	17167.35	537.3992
$Z_{earthworm}$ ((lipid$\cdot K_{ow} \cdot \rho_{earthworm}$)/H)	239.9001	9905.181	214.327
$C_{soil\ water}$ (mg/L)	0.117696	0.001131	0.007609
ρ_{soil} (g/cm³)	1.3	1.3	1.3
$\rho_{earthworm}$ (g/cm³)	1	1	1
θ (unitless)	0.3	0.3	0.3
ε (unitless)	0.5	0.5	0.5
K_{aw} (H/RT)	0.000178	0.0000026	0.000053
K_{bw} (($\rho_{soil} \cdot$Kd)+θ+(ε-θ)(K_{aw}))	19.20204	109.656	70.96801
Earthworm Concentration (mg/kg)	25.08	0.14	0.43
Robin Oral Dose (mg/kg-bw/day)	0.72	0.02	0.09
Quail Oral Dose (mg/kg-bw/day)	0.26	0.01	0.06
Meadow Vole Oral Dose (mg/kg-bw/day)	0.25	0.01	0.06

*Concentrations are based on in-furrow spray application to surface at 44 mg/ft²

For chronic fipronil and degradates oral dose exposures to the robin, bobwhite quail, and meadow vole, a 20-week average concentration of each compound immediately following application was calculated in soil over 1 cm and 15 cm depth profiles. Twenty weeks was selected as the averaging period to be consistent with the exposure durations encountered in available rat multi-generation and avian reproduction toxicity studies. Table 6 summarizes these estimated soil concentrations.

Table 6. Estimated Soil Concentrations for Fipronil and Degradates In-Furrow Application (20-Week Average Soil Concentrations*)

Chemical	Soil Concentration (mg/kg) ca 1 cm	Soil Concentration (mg/kg) ca 15 cm
fipronil	22.04	1.55
MB45950	1.55**	0.11
MB46136	7.45***	0.49

* 20-week average assumes $t_{1/2}$ of 128 days
** assumes a 5% conversion efficiency
*** assumes a 24% conversion efficiency

Using the 20-week average soil concentrations in the avian and mammalian receptors yields the following estimated maximal year one chronic oral dose estimates (Table 7).

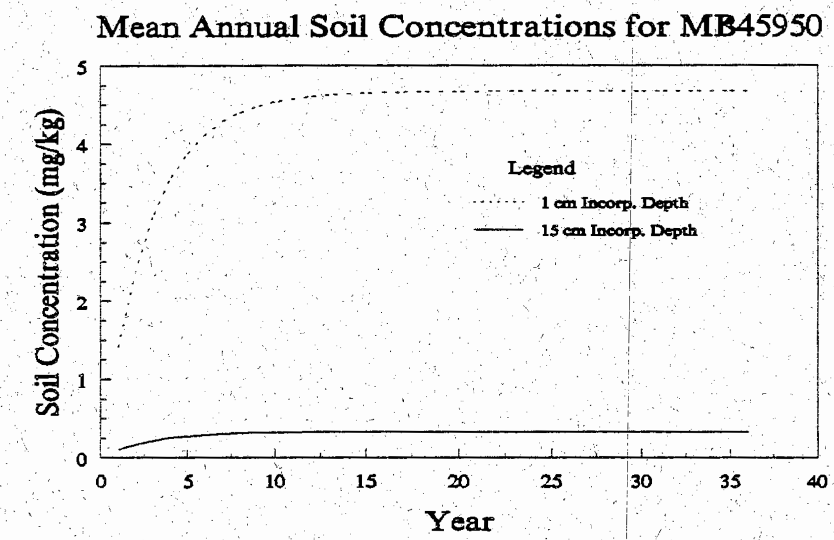
Table 7. Chronic Oral Dose Estimates for Avian and Mammalian Receptors (Maximum Year 1 20-Week Average)

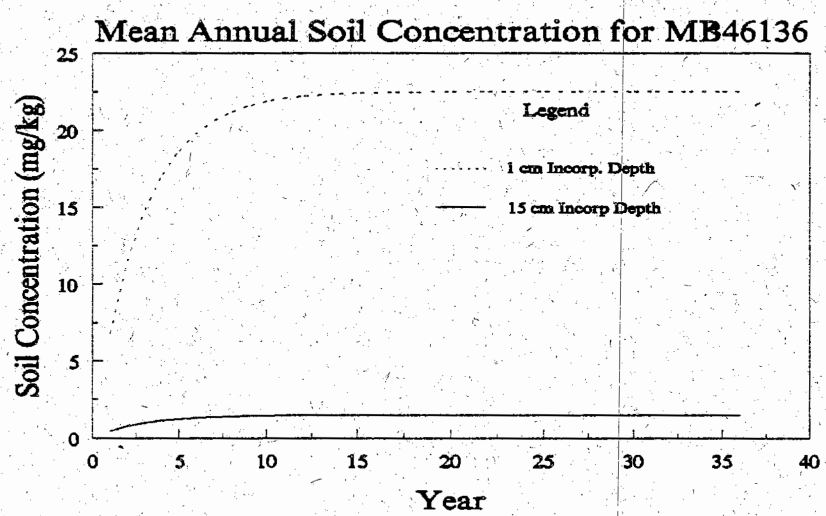
Receptor	Fipronil Chronic Dose (mg/kg-bw/day)	MB45950 Chronic Dose (mg/kg-bw/day)	MB46136 Chronic Dose (mg/kg-bw/day)
Robin	0.48	0.018	0.082
Bobwhite quail	0.17	0.012	0.058
Meadow vole	0.16	0.011	0.055

Multiple Year Considerations

It should be emphasized that the dietary exposure estimates for avian and mammalian receptors are for the first year of treatment only. The environmental stability of fipronil degradates suggests that there will be carry-over of annual application residues from year to year. With additional consecutive applications of fipronil to corn fields, it is likely that fipronil degradate concentrations in years following the initial application will increase. Figure 3 presents the impact of multiple-year applications of fipronil on the concentration of degradates in soil over the 1 cm and 15 cm depth profiles used in the exposure assessment. This data (generated on the assumption that degradate half-lives are on the order of 700 days) indicate that 1 cm depth fipronil concentrations are likely to accumulate to levels substantially greater that those estimated for the first year of application. More refined and less uncertain estimates of this multiple year accumulation phenomena would require additional information with respect to the aerobic soil metabolism of fipronil degradates.

Figure 3. Accumulation Profiles for Fipronil Degradates in Soils after Repeated Annual Application to Corn Fields





C. Ecological Hazard Potential for Non-Target Organisms

Mode of Action

According to the manufacture's data, fipronil affects the gamma-aminobutyric acid neurotransmission system by interfering with the passage of chloride . In addition, research data indicate that fipronil displays a higher potency in the insect GABA chloride channel than in the vertebrate GABA chloride channel which may indicate selective toxicity (Hainzl and Casida 1996).

Terrestrial Organism Toxicity

Mammalian Toxicity Data

Wild mammal testing is required on a case-by-case basis, depending on the results of the lower tier studies such as acute and subacute testing, intended use pattern, and pertinent environmental fate characteristics. In most cases, however, an acute oral LD_{50} from the Agency's Health Effects Division (HED) is used to determine toxicity to mammals (HED Tox One-liners). These $LD_{50's}$ are reported in Table 8. The available mammalian data indicate that fipronil (Technical) is moderately toxic to small mammals on an acute oral basis. The 1.6% in EXP60655A and 0.25% in RM1601C formulations of fipronil did not demonstrate significant mammalian dietary toxicity.

Table 8. Mammalian Acute Oral Toxicity Findings

Species	% AI	LD_{50} (mg/kg-bw)	MRID	Category
Rat (small mammal)	93%	97	429186-28	Mod. Toxic
Rat (small mammal)	MB46136 degr.(98%)	218	429186-75	Mod. Toxic
Rat (small mammal)	1.6(form.) EXP60655A	>5000	429186-36	P.Non-Toxic
Rat (small mammal)	0.25(form.) RM1601c	>5000	431211-04	P.Non-Toxic

Fipronil and desulfinyl fipronil (MB46513) were evaluated for persistence and metabolism in male Swiss-Webster mice as well as comparative acute toxicity (intraperitoneal administration) and affinity for the mouse GABA receptor (Hainzl and Casida, 1996). Groups of mice received five daily 1 mg/kg doses of fipronil or MB46513, i.p. Mice were sacrificed at day 6 and day 27 and adipose tissue was analyzed for fipronil and degradates. Adipose tissue of fipronil treated mice contained only the sulfone metabolite of fipronil (MB46136). MB46513 treated mice contained only this photodegradate in adipose tissue, suggesting no metabolism of the compound. Adipose concentrations of MB46136 and MB46513 were at a maximum at day 6 (22-24 mg/kg fat) but by day 27 these concentrations had been reduced to 0.8 to 3.2 mg/kg. The neurotoxic potency of fipronil was maintained or possibly increased upon the formation of desulfinyl derivatives of fipronil. The acute i.p. LD_{50} for fipronil in mice was 41 mg/kg, while the LD50 for MB46513 was 23 mg/kg, suggesting the potential for comparable toxicity between fipronil and the photodegradate in mammalian systems. It is noteworthy that MB46513 exhibits a greater affinity for the mouse GABA receptor (IC_{50} 94 nM) than parent fipronil (IC_{50} 1010 nM). The toxicity data and GABA receptor data suggest that risk assessments for uses of fipronil where the photodegradate can be expected to be produced should assess the potential toxicological implications of this degradate.

A number of toxicological studies involving subchronic and chronic exposure of mice, rats, and dogs to fipronil are available. These studies address a variety of toxicological endpoints including neurological function, thyroid function, carcinogenicity, histology, reproductive effects, and developmental effects. EFED has concentrated the toxicological evaluation of effects on mammalian systems to those effect endpoints expected to be of the highest ecological relevance. Concern for wild mammal population maintenance focused this evaluation on effects to individual fecundity and survivability of offspring. Therefore, EFED has concentrated on reproductive and developmental endpoints. A multi-generation reproduction study in CD rats (MRID 429186-47) is the source of reproductive toxicity data for this assessment. Thirty-six CD rats/sex/group received fipronil continuously in the diet at concentrations of 0, 3, 30, and 300 mg/kg diet. This study reported decreased litter size in F_1 and F_2 litters and a decrease in the percentage of F_1 parental animals mating at the maximum dose tested 300 mg/kg-diet. In addition, this high dose produced reduced post-implantation and postnatal survivals in F_2 litters. The NOEL for these effects is 30 mg/kg-diet (HED equivalence to 2.54 mg/kg-bw males, 2.74 mg/kg-bw females) and the LOEL is 300 mg/kg-diet (HED equivalence to 26.03 mg/kg-bw males, 28.4 mg/kg-bw females).

Avian Toxicity Data

Table 9 summarizes the acute oral toxicity data for birds exposed to fipronil. The oral toxicity to fipronil is extremely variable among species tested. Fipronil is very highly toxic to bobwhite quail, partridge, and pheasant, yet nearly non-toxic to the pigeon, house sparrow, and mallard duck. The degradate MB 46513 is 2 times more orally toxic to bobwhite quail than the parent compound and was 4 times more orally toxic to the mallard duck.

Table 9. Avian Acute Oral Toxicity Findings

Species	% A.I.	LD_{50} (CLs) (mg/kg-bw)	NOEC (mg/kg-bw)	MRID No. Author/Year	Classification
Northern bobwhite	96	11.3* (9-14)	< 4	429186-17 Pedersen (1990)	Core
Mallard duck	96.8	>2150	2150	429186-16 Pedersen(1990)	Core
Pigeon	97.7	>500	N.R.	429186-13, Hakin and Rodgers(1991)	Supplemental
Red-legged partridge	95.4	34 (28-42)	16	429186-14 Hakin and Rodgers(1992)	Supplemental
Pheasant	95.4	31 (22-44)	5	429186-15 Hakin and Rodgers(1992)	Supplemental
House sparrow	96.7	1000 (742-1691)	<464	429186-18 Pedersen and Helsten(1991)	Supplemental
Northern bobwhite	99.7 MB46513	5 (2.4-12)	3.16	437766-01 Pedersen and Solatycki(1993)	Supplemental
Mallard duck	98.6 MB46513	420 (298-581)	147	437766-02 Helsten and Solatycki(1994)	Supplemental
Northern bobwhite	1.6 WG	1065 (700-1400	175	429186-19 Pedersen and DuCharme(1993)	Supplemental

* 30% mortality at 10 mg/kg-bw and 0% mortality at 4.6 mg/kg-bw. NOEL=1 mg/Kg

Table 10 summarizes the available avian subacute dietary toxicity data. Fipronil is very highly toxic to bobwhite quail on a subacute dietary basis, yet is practically non-toxic to mallard duck on a subacute basis. The dietary toxicity assessment is based on less extensive data set than the acute oral toxicity assessment. Therefore, it is not certain whether the wide species sensitivity seen in oral testing would also be displayed in dietary studies. The reviewer assumes that this is a possibility that must be considered in assessing potential risk. In addition, there are no dietary toxicity data for fipronil degradates. Because the oral toxicity to bobwhite was higher for MB 46513 than for fipronil, the Agency is also concerned that dietary toxicity may be higher for other metabolites of fipronil.

Table 10. Avian Subacute Dietary Toxicity Findings

Species	% A.I.	LC_{50}(CLs) (mg/kg-diet)	NOEC (mg/kg-diet)	MRID No. Author/Year	Classification
Northern bobwhite	95% Tech.	48.0 (38-59)*	19.5	429186-20 Pedersen(1993)	Core
Mallard duck	95% Tech.	>5000(N.A.)	1250	429186-21 Pedersen(1993)	Core

* 20% mortality at 35 ppm and 0% mortality at 16 ppm(NOEL).

The avian reproductive studies (Table 11) indicate that fipronil had no effects at the highest levels that were tested in mallard (NOEC=1000 mg/kg-diet) and bobwhite quail (10 mg/kg-diet). The bobwhite NOEC of 10 ppm, which was the highest level tested, will be used as the chronic effects regulatory endpoint pending further studies for terrestrial avian species. The quail study does not fulfill guideline requirements, and the need for a new study is apparent unless the present proposed use will not produce terrestrial EECs above 10 mg/kg-diet. Based on estimated residue levels for in furrow use on corn, the current study will be adequate. Using body weight and feed consumption data for the 10 mg/kg-diet exposure the mean bodyweight over the course of the study was 209.1 g (0.2091 kg) and the mean food consumption rate was 18.3 g/day (0.0183 kg/day). Applying these two mean values to the dietary NOEC of 10 mg/kg-diet, yields an oral dose NOEL estimate of 0.88 mg/kg-bw/day. Estimation of this NOEL is necessary for assessing risk through the oral consumption of fipronil and its degradates from in-furrow spray applications.

Table 11. Avian Reproductive Toxicity Findings

Species	% A.I.	NOEC (mg/kg-diet)	LOEC (mg/kg-diet)	Endpoint Affected	MRID No. Author/Year	Classification
Northern bobwhite	96.7 Tech.	10	Not Determined	None	429186-22 Pedersen and DuCharme(1993)	Supplemental
Mallard duck	96.7 Tech.	1000	>1000	None	429186-23 Pedersen and Lesar (1993)	Core

Aquatic Organism Toxicity

Tables 12 and 13 summarize the data reviewed to date using fipronil technical, and fipronil degradates which are expected to persist in the aquatic environment. In order to establish the toxicity of a pesticide to aquatic organisms certain data are required using the technical grade of the active ingredient. Two freshwater fish toxicity studies(with one study using a coldwater species (preferably the rainbow trout) and the other a warmwater species (preferably the bluegill sunfish) are required. A freshwater aquatic invertebrate toxicity test(preferably using first instar *Daphnia magna* or early instar amphipods, stoneflies, mayflies, or midges) is required. When an end-use product is intended for direct application to the marine/estuarine environment or is expected to reach this environment in significant concentrations three acute toxicity tests (fish, mollusc, and crustacean) with estuarine and marine organisms are required. If the test substance is expected to persist in aquatic environments then early life stage testing with fish(freshwater and/or marine) and lifecycle testing with invertebrate species (freshwater and/or marine) is required.

The results of the 96-hour acute toxicity studies (Table 12) indicate that fipronil (Technical) and MB46136 degradates are very highly or highly toxic to bluegill sunfish, rainbow trout and sheepshead minnow (estuarine). The metabolites RPA 104615 and MB46513 appears to be nearly non-toxic to fish.

Table 12. Freshwater and Marine Fish Acute Toxicity Findings

Species	% A.I.	LC_{50} (CLs) (µg/L)	NOEC (µg/L)	MRID No.	Classification
Freshwater Species					
Bluegill sunfish	100 Tech.	83(72-98)	43	429186-24	Core
Rainbow trout	100 Tech.	246(205-342)	34	429779-02	Core
*Rainbow trout	99.2-deg. (MB46136)	39(34-43)	18	429186-73	Supplemental
*Bluegill sunfish	99.2 deg. (MB46136)	25(21-30)	6.7	429189674	Supplemental
*Rainbow trout	94.7 photo-degr. (RPA104615)	>100,000	NA	432917-18	Supplemental
*Rainbow trout	MB46513	>100,000	36,000	43279703	Core
Marine/Estuarine Species					
Sheepshead minnow	96.1 Tech.	130(110-280)	<110	43291702	Core

* Studies used aerobic metabolic degradates/metabolites of Fipronil.

Data from fish early life-stage tests (Table 13) were required for fipronil due to the high acute toxicity of the parent, persistence characteristics, and the probability fipronil will enter bodies of water from the proposed use on corn. The results indicate that fipronil affects larval growth at concentrations greater than 6.6 µg/L, but less than 15 µg/L in rainbow trout.

Table 13. Fish Early Life-Stage Toxicity Findings

Fish Early Life-Stage Toxicity Findings						
Species Tested	% A.I.	NOEC (µg/L)	LOEC (µg/L)	MRID Author/Year	Endpoints Affected	Category
Rainbow trout	96.7 Tech.	6.6	15	429186-27 Machado(1992)	Larval length	Core

There is sufficient information to characterize fipronil parent and its degradates MB46136 and MB45950 as very highly toxic to aquatic invertebrates (Table 14). The RPA 104615 appears to be nearly non-toxic to daphnids.

Table 14. Freshwater Invertebrate Acute Toxicity Findings

Species Tested	% A.I.	48-h EC_{50} (μg/L)	MRID NO. Author/Year	Classification
Daphnia magna	100 Technical	190	429186-25 McNamara(1990)	Core
Daphnia magna (see 21 Day study)	100 % technical	39 (21 Day)	429186-26 McNamara(1990)	Supplemental
Daphnia magna	*94.7 photodeg. RPA 104615	100,000	432917-19 Collins(1992)	Supplemental
Daphnia magna	100% MB 46136 degradate	29	429186-71 McNamara(1990)	Supplemental
Daphnia magna	*100% MB 45950 degradate	100	429186-69 McNamara(1990)	Supplemental

* studies used different degradates/metabolites of fipronil.

Because fipronil is proposed for use on crops which may be located adjacent to estuarine habitats, aquatic invertebrate testing with estuarine marine invertebrate species was required. Table 15 summarizes the results of these studies. There is sufficient information to characterize fipronil as highly toxic to oysters and very highly toxic to mysids.

Table 15. Estuarine/Marine Invertebrate Acute Toxicity Results

Species	% A.I.	LC_{50}/EC_{50} (CIs) (μg/L)	MRID No. Author/Year	Classification
Eastern oyster	96.1	EC50=770 (180-1700)	432917-01 Dionne/1993	Core
Mysid	96.1	EC50=0.14 (0.12-0.16)	432797-01 Machado/1994	Upgraded to core

Data from aquatic invertebrate life cycle tests are required due to persistence of fipronil in water, high acute toxicity and the probability that the compound will enter bodies of water from the proposed use on corn (Table 16).The results indicate that fipronil affects growth in daphnids at concentrations exceeding 9.8 μg/L (MRID 42918626). The results also indicate that fipronil affects reproduction, survival and growth of mysids at concentrations less than 0.005 μg/L (MRID 436812-01). The mysid study does not meet guideline requirements because effects occurred at all test concentrations and an NOEC was not determined. The daphnia study does not meet guideline requirements because of high mortality in the dilution water control and high variability in the analytical measurements. Both studies with daphnids and mysids indicate that chronic exposure to fipronil may result in toxic effects at water concentrations substantially below acute effect levels. This potential for chronic effects and the persistence of fipronil suggest that the mysid and daphnid chronic studies should be repeated to support full registration of fipronil on cotton, corn, and rice.

Table 16. Aquatic Invertebrate Chronic Life-Cycle Toxicity Findings

Species Tested	% A.I.	LOEC/NOEC (µg/L)	MRID No. Author/Yr	Endpoints Affected	Classification
Mysid	97.7 Tech	LOEC 0.005 NOEC not determined	436812-01 Machado/1995	Survival Reproduction and Growth	Supplemental
Daphnia magna	100 Tech	LOEC 20 NOEC 9.8	429186-26 McNamara/1990	Length	Supplemental

Toxicity to Non-Target Beneficial Insects

Interim data (Table 17) suggest that fipronil is extremely toxic to honeybees via direct contact or oral ingestion of fipronil residues. The Agency has not reviewed data regarding the acute or foliar contact toxicity of fipronil to honeybees or other non-target beneficial insects. Because fipronil is applied as in furrow insecticide with a low probability of exposure to non-target beneficial insects, the honey bee toxicity tests are not needed to support in-furrow uses of fipronil. However, the study will be needed to support foliar groundspray and aerial application of fipronil.

Label warnings do advise that fipronil is highly toxic to honeybees so it is assumed that studies have been conducted but not submitted to the Agency. Interim toxicity endpoints are listed in the table below.

Table 17. Toxicity to Nontarget Beneficial Insects

Species	Study Type	Toxicity (µg ai/bee)	MRID Study Date	Category
Apis mellifera	Acute contact	LD50: 0.00593	N/A	Unverified
Apis mellifera	Acute oral	LD50: 0.00417	N/A	Unverified
Apis mellifera	Foliar contact	No data	No data	

Toxicity to Plants

Generally the Agency does not require terrestrial or aquatic plant testing for insecticide products. However, Tier I aquatic plant testing was provided due the probability that drift to aquatic habitats will occur from aerial applications to cotton. Table 18 presents the available data for 5 aquatic plant species. Based on the limited data aquatic plant species are not expected to beadversely effected at concentrations of up to 100 µg/L.

Table 18. Nontarget Aquatic Plant Toxicity Findings

Species Tested	% A.I.	5 Day EC50 (µg/L)	MRID # Author/year	Classification
Navicula pelliculosa (FW diatom)	96.1	>120	42918658 Hoberg/1993	Core
Lemna gibba (Duckweed)	96.1	>100	42918656 Hoberg/1993	Supplemental
Selenastrum capricornutum (FW green alga)	96.1	140	42918660 Hoberg/1993	Core
Skeletonema costatum (marine diatom)	96.1	>140	42918659 Hoberg/1993	Core
Anabaena flos aquae (FW Blue-green alga)	96.1	>170	42918657 Hoberg(1993)	Core

D. Ecological Risk Assessment

Avian and Mammalian Risk Assessment

Likelihood of Exposure

Characterization of risk to non-target species is based on the expected environmental concentrations, the potential for exposure to non-target organisms from the proposed use and the known toxicity levels of this compound and it's degradates to the various species expected to be exposed in these agricultural settings. Based on the large acreage represented by corn production and the diversity of species found near these areas, a large number of terrestrial and aquatic species are likely to be potentially exposed.

Avian and Mammalian Granular Exposure Risk Assessment

For granular pesticides the exposure is represented by the amount of active ingredient in a square foot area. This exposure value is then compared to the LD_{50} of the most sensitive test species to derive the risk quotient of an LD_{50} per square foot.

The LD_{50} per square foot for granular fipronil was based on T-Band and In-Furrow application rates (band width 7 inches for T-Band and 1 inch for in-furrow) of 8 ounces REGENT 1.5G per 1000 row feet. This is equivalent to 8.7 lbs of product per acre (0.13 lbs ai/acre) based on a 30-inch row spacing. As indicated in EPA's Risk Analysis for Granular Pesticides, the T-Band and In-Furrow application techniques are likely to leave 8% and 1%, respectively, of the applied granules on the surface and available to birds and mammals. These percentages are incorporated in the calculations. Maximum allowable amount applied per growing season is 4.4(3.0G) to 8.7(1.5G) pounds of the granular products per acre (equivalent to 0.13 lbs ai/acre). The product is only applied at planting.

Calculation for Number of Avian LD_{50} per Square Foot T-Banded Application with Incorporation

Product (oz)/1000 row ft x % A.I. x 28349 mg/oz

8 oz./1000 row ft x 0.015(1.5% A.I.) x 28349 mg/oz=3401
1000 ft x bandwidth (ft) = 3401 mg /1000 ft of row x 0.583ft
Result=5.84 mg A.I./sq.ft.

A.I.(mg)/sq.ft. x % unincorporated = Exposed A.I. mg/sq.ft.
5.84 x 8% = 0.47 mg ai/ft^2(T-Band)

Exposed A.I. mg/ft^2 0.47
LD_{50} X Wgt. of Bird (kg) 11.3 x .178 kg = 0.23 LD_{50} /ft^2

Calculation for Number of Avian LD_{50} per Square Foot In-Furrow Application with incorporation

Product (oz)/1000 row ft x % A.I. x 28349 mg/oz =

8 oz. x 0.015 x 28349 mg/oz = 40.99 a.i.(mg)/sq.ft.

1000 ft x bandwidth (ft) = 1000 x 0.083 =83 1 inch=0.083 ft
A.I. (mg)/sq.ft. x % unincorporated = Exposed A.I. mg/sq.ft.
40.99 mg/sq ft. x 1% = 0.41 mg/ft^2(In-furrow)
Exposed A.I. mg/ft^2 0.41
LD_{50} X Wgt.of Bird (Kg) 11.3 x 0.178 kg

Result = 0.20 LD_{50} /ft^2

The proposed use of fipronil on corn does not exceed the criteria for high risk ($LD_{50}/ft^2 \geq 0.5$) to avian species for T-Band and In-furrow granular application methods. However, the (LD_{50}/ft^2. for both methods does meet the criteria for Restricted Use Classification ($LD_{50}/ft^2 \geq 0.2$). These results are based on the bobwhite quail, the most sensitive species tested. The toxicity data indicate that degradate MB46513 is also very highly toxic to birds, with an LD_{50} value of 5 mg ai/kg-bw. Substituting this value in the above equations gives LD_{50}/ft^2 values of 0.53 (T-Band) and 0.46 (In-Furrow). These LD_{50}/ft^2. values exceed or nearly reach our criteria for high acute risk. It should be noted that accumulation of MB46513 is possible because of its high persistence in terrestrial environments.

EFED currently has no methodology for assessing risks to small mammal populations from exposure to pesticides in granular formulation. Similarly, there currently is no methodology for assessing chronic reproductive risks to birds from exposure to granular pesticides.

Avian and Mammalian Risk Assessment from Exposure to In-Furrow Spray Residues

Acute Risks

Maximal oral dose estimates of exposure for robins, bobwhite quail, and meadow voles were compared with available acute toxicity (LD_{50}) data. The LD_{50} for bobwhite quail was used as a estimate of the potential toxicity of fipronil to robins and bobwhite quail. In the absence of acute toxicity data specific to the robin, this is a conservative approach for assessing the toxicity of fipronil to this species. Fipronil and degradate toxicity to the meadow vole was estimated using toxicity data for laboratory rats. Because acute avian toxicity data were not available for the degradates of concern (MB45950 and MB46136), the toxicity data for fipronil were used to represent the potential toxicity of degradates to avian species. Available data for the photodegradate MB46513 suggests that degradates possessing the F_3C- moiety of the parent compound may be as least as toxic as parent fipronil. Similarly, the absence of acute toxicity data for MB45950 necessitated an assumption that this degradate was similar in toxicity to parent fipronil. Table 19 summarizes the estimation of acute Risk Quotients for avian and mammalian species potentially exposed to fipronil and degradates as a result of in-furrow spray applications.

Table 19. Acute Dietary Risk Quotients for Avian and Mammalian Terrestrial Receptors

Species	Acute Toxicity* (mg/kg-bw)	Oral Dose Estimate (mg/kg-bw/day)	Acute Dietary Risk Quotient (In-Furrow Spray)
American Robin	fipronil LD50 11.3	0.72	0.06
	MB45950 LD50 11.3**	0.02	0.002
	MB46136 LD50 11.3**	0.09	0.008
Bobwhite Quail	fipronil LD50 11.3	0.26	0.02
	MB45950 LD50 11.3 **	0.01	0.001
	MB46136 LD50 11.3 **	0.06	0.005
Meadow Vole	fipronil LD50 97	0.25	0.003
	MB45950 LD50 97 **	0.01	0.0001
	MB46136 LD50 218	0.06	0.0003

* Toxicity for robin is conservatively based on bobwhite quail, the most sensitive species tested. Toxicity for meadow vole is based on toxicity data for laboratory rats.

**In the absence of toxicity data to the contrary, the toxicities of degradates were assumed to be equivalent to parent fipronil. This assumption was based on the presence of the biologically active F_3C- moiety on degradates, the structural moiety indicated by the registrant as the biologically active structure responsible for fipronil toxicity.

The Risk Quotients comparing acute LOCs to estimated dietary exposures to fipronil and its degradates in soil and soil invertebrates for two representative bird species (robin and bobwhite quail) are orders of magnitude below 1. In-furrow spray applications of fipronil do not appear to pose an acute risk to avian species. Similarly fipronil's proposed use on corn does not appear to present an acute risk to small mammals similar in size and sensitivity to the rat. Incidental exposures to fipronil and its degradates in soil are orders of magnitude below acute mammalian LOCs at proposed rates for corn use.

Chronic Risks

Estimated soil concentrations of fipronil and degradates averaged over the first 20 week period following an in-furrow spray application were used to estimate chronic oral dose exposures for robins, bobwhite quail, and meadow voles through consumption of soil and soil invertebrates. These 20 week average concentrations were then compared to available chronic LOCs for birds and mammals. As discussed in the toxicological review section of this assessment, the NOEL (26.03 mg/kg-bw/day) for reduced litter size, reduced weanling survivability, and reduced mating from a rat multi-generational reproductive study serves as the LOC for the chronic mammalian assessment of risk. For avian species, the reproductive data is for bobwhite quail showed no effects at a dietary concentration of 10 mg/kg. This dietary concentration is equivalent to an oral dose exposure of 0.88 mg/kg-bw/day, which is used as the chronic LOC for avian species. Table 20 summarizes the chronic Risk Quotients derived by this comparison.

Table 20. Chronic Dietary Risk Quotients for Avian and Mammalian Terrestrial Receptors

Species	ChronicToxicity* (mg/kg-bw)	Oral Dose Estimate (mg/kg-bw/day)	Chronic Dietary Risk Quotient (In-Furrow Spray)
American Robin	fipronil NOEL 0.88	0.48	0.55
	MB45950 NOEL 0.88 **	0.018	0.02
	MB46136 NOEL 0.88 **	0.082	0.09
Bobwhite Quail	fipronil NOEL 0.88	0.17	0.19
	MB45950 NOEL 0.88 **	0.012	0.01
	MB46136 NOEL 0.88 **	0.058	0.07
Meadow Vole	fipronil NOEL 26.03	0.16	0.006
	MB45950 NOEL 26.03 **	0.011	0.0004
	MB46136 NOEL 26.03**	0.055	0.002

* Toxicity for robin is conservatively based on bobwhite quail, the most sensitive species tested. Toxicity for meadow vole is based on toxicity data for laboratory rats.

**In the absence of toxicity data to the contrary, the toxicities of degradates were assumed to be equivalent to parent fipronil. This assumption was based on the presence of the biologically active F_3C- moiety on degradates, the structural moiety indicated by the registrant as the biologically active structure responsible for fipronil toxicity.

Risk Quotients comparing 20-week estimated maximum oral doses (year 1 of application) with reproduction-based chronic LOCs for robins, bobwhite quail, and meadow voles are all less than 1. Based on these risk quotients, first year application of fipronil by in-furrow spray do no pose a chronic risk to avian and mammalian species expected to use corn fields as a dietary source area.

Aquatic Risk Assessment

Likelihood of Exposure

Fipronil displays high toxicity to most aquatic organisms tested to date. The large multi-state area that may be encompassed by this use pattern will undoubtedly include sites which are adjacent to irrigation canals, streams, ponds, rivers, lakes and estuarine habitats. Thus, the aquatic species diversity which is potentially at risk to exposure from runoff is large.

Aquatic Risk Quotients for Use Classification for Fipronil for Granular and Ground Spray Methods of Application

The acute and chronic risk quotients (RQ) for freshwater and estuarine organisms based on technical fipronil are summarized in Table 21. The application scenario is a single 10 ha application at 0.13 lbs ai/acre with incorporation to 1 inch depth.

Estimated peak surface water concentrations of fipronil and MB46136 exceeded acute LOCs for estuarine invertebrates (i.e. mysid). In addition, estimated time-weighted surface water concentrations (averaged over time periods consistent with chronic endpoints) for fipronil, MB46136 and MB45950 exceeded the chronic LOCs. These comparisons suggest that fipronil and degradates pose both acute and chronic risks to estuarine invertebrates.

Table 21. Acute and Chronic Risk Quotients for Freshwater and Estuarine Organisms

Most Sensitive Species Group Tested	Levels of Concern Acute (LC_{50}) Chronic (NOEC) (µg/L)	Peak EEC* (µg/L)	Chronic EEC* (µg/L)	Maximum Acute RQ's	Maximum Chronic RQ'S
Fipronil					
Freshwater Fish 429186-24	LC50=83 NOEC=6.6 LOEC=15 (parent)	0.71	0.276 (56-day)	0.008	0.04
Freshwater Invertebrate 42918625	EC50=190 NOEC=9.8 LOEC=20 (parent)	0.71	0.5 (21-day)	0.0035	0.05
Estuarine Crustacea 432797-01	LC50=0.14 NOEC<0.005 LOEC=0.005 (parent)	0.71	0.5 (21-day)	5.05	>100
Estuarine Mollusc 432917-01	EC50=770 (parent)	0.71	0.5 (21-day)	0.0009	No Tox Data
Estuarine Fish 432917-02	LC50=130	0.71	0.276 (56-day)	0.005	No Tox Data
Degradate MB46136					
Freshwater Invertebrate 429186-71 (chronic value estimated by application of fipronil ACR)	EC50=29 NOEC=1.5 LOEC3.05	0.168	0.1 (21-day)	0.0001	0.07
Freshwater Fish 429186-74 (chronic value estimated by application of fipronil ACR)	LC50=25 NOEC1.98 LOEC=4.52	0.168	0.062 (56-day)	0.0002	0.014
Mysid toxicity (assumed equivalent to fipronil)	LC50=0.14 NOEC<0.005 LOEC=0.005	0.168	0.1 (21-day)	1.2	>20
MB45950					
Freshwater Fish (assumed acute and chronic equivalent to fipronil)	EC50=83 NOEC=6.6 LOEC=15	0.039	0.027 (21-day)	0.0005	0.004
Freshwater Invertebrate (chronic value estimated by application of fipronil ACR)	EC50=100 NOEC=5.16 LOEC=10.52	0.039	0.019 (56-day)	0.0004	0.0037
Mysid toxicity (assumed acute and chronic equivalent to fipronil)	LC50=0.14 NOEC<0.005 LOEC=0.005	0.039	0.027 (21-day)	0.28	>5.4

* Peak and chronic EECs for fipronil are based on PRZM/EXAMS. PEAK and chronic EECs for degradates are based on GENEEC. Although PRZM/EXAMS modeling was conducted for fipronil degradates, the one-in-ten year EECs were not used because accumulation was observed.

Aquatic Plant Risk

The EC_{50} for the aquatic plant species tested to date and the estimated aquatic concentrations from the proposed use on corn will not exceed acute toxicity levels for aquatic plants.

Nontarget Beneficial Insect Risk

The Agency cannot characterize the risk of adverse impacts to beneficial insects from application of fipronil insecticide products. It is assumed that hazardous impacts to honeybees and other beneficial insects are unlikely if fipronil is properly incorporated. It is also assumed that fipronil has been tested by the registrant and found to be highly toxic to honeybees as there is a label statement to this effect on the REGENT 80 WG label. Impacts to beneficial soil invertebrates, such as earthworms, are probable given the mode of action for fipronil and it's incorporation into soils.

Endangered Species Concerns

Fipronil use on corn does offer potential acute hazard to sensitive endangered avian species feeding in corn fields. Within the corn field insectivorous birds and small mammals, such as field mice or voles, feeding on emerging insects near treated furrows may be subject to ingestion of potentially harmful residues. Avian sensitivity is expected to be extremely species dependent as it was with bobwhite and mallard. The deeper the incorporation of granules or sprayed soils, the less likelihood of avian or mammalian exposure. This is particularly important on bare, recently plowed soils which often attract avian species due to ease of locating exposed soil invertebrates.

The use of fipronil on corn is expected to offer potential hazard to endangered aquatic invertebrates located in surface or subterranean waters. Little breakdown is expected if fipronil reaches underground water systems due to the absence of the primary source of degradation: exposure to sunlight. Shallow stream organism may be less effected if waters are clear, rapidly moving, and exposed to sunlight. Concentration in shaded pools could cause a exposure to potentially hazardous residues for sensitive listed species of invertebrates.

The Endangered Species Protection Program is expected to become final sometime in the near future. Limitations in the use of Fipronil may be required to protect endangered and threatened species, but , these limitations have not been defined and may be formulation and location specific. EPA anticipates that a consultation with the Fish and Wildlife Service will be conducted in accordance with the species-based priority approach described in the Program. Modifications would most likely consist of the generic label statement referring pesticide users to use limitations contained in county bulletins. For the present, the reviewer has included a listing of endangered species likely to be exposed and possibly vulnerable to the proposed uses of fipronil on corn. This listing is included as a reference for potential risk mitigation on a case-by-case basis.

Adequacy of Ecological Toxicity Data

Though the registrant has submitted an extensive data set for this pesticide, questions still remain concerning the long term effects to the environment from use of Fipronil products. To date, there has been no data submitted to characterize toxicity of fipronil to non-target insects. Avian reproductive testing for the gamebird species does not allow conclusions regarding safety from chronic effects above a 10 ppm residue level. Dietary toxicity of metabolites to avian wildlife species is unknown, though it may be higher than the parent compound based on the oral toxicity relationship of the parent and MB46513 metabolite. The lack of data to answer these questions may hinder a proper risk assessment for future uses. The characterization of possible sublethal effects to fish is complicated by the fact that the degradate MB46136 is 4 times more acutely toxic to trout than the parent compound and is expected to persist in the environment. Possible effects to second generation fish from the parent or the degradates cannot be assessed due to the lack of a full fish life-cycle study.

E. Environmental Risk Characterization

Summary

The risk assessment indicates that in-furrow use of fipronil, formulated as REGENT 1.5G, 3G, 80WG and 4SC, on corn is likely to pose risk to gallinaceous birds (*i.e.*, bobwhite quail and pheasant) from ingestion of exposed granular fipronil. In addition, the high toxicity of fipronil and its degradates, compared to estimates of surface water concentrations from runoff, suggest toxicological risks to aquatic invertebrates in estuarine systems. Fipronil and its degradates did not exceed acute toxic levels of concern for small mammal species, freshwater fish, or freshwater invertebrates. Fipronil degrades to form metabolites of potential toxicological concern (MB46136, MB46513, and MB45950). These metabolites are assumed to be equally toxic as parent fipronil because they contain the same toxic moiety (CF_3-) as fipronil. The environmental fate data indicate that fipronil and its degradates have a moderate soil sorption affinity and moderate to high persistence in terrestrial and aquatic environments. Because fipronil residues exhibit a high environmental persistence , there is a high potential for accumulation in terrestrial and aquatic environments. Accumulation of fipronil residues (particularly fipronil degradates) is likely to result in long-term exposure. In-furrow application of fipronil, however, is expected to limit exposure, which is expected to reduce direct exposure to fipronil granules and to reduce the potential for fipronil movement in runoff waters.

Environmental Fate Characterization

The environmental fate data for fipronil are generally acceptable to formulate a comprehensive fate and transport assessment. However, a major limitation in the fipronil environmental fate assessment is the low confidence level associated with data on the persistence of fipronil in aquatic environments. Soil and aquatic metabolism studies provide contradictory data on fipronil persistence to microbially-mediated degradative processes. The registrant should provide a complete explanation on disparate half-lives reported for fipronil in aquatic and soil metabolism studies. The environmental fate assessment for fipronil metabolites is more uncertain because of the lack persistence data in terrestrial and aquatic environments. Data gaps force an assumption of high persistence for environmental fate and transport modeling. EFED notes that interim data were used in the risk assessment for MB 46136 and MB 45950. A complete review of the interim photodegradation and batch equilibrium data are needed to substantiate the validity of the data. Therefore, EFED reserves judgment on data acceptability pending a complete data evaluation.

Fipronil is moderately persistent to persistent ($t_{1/2}$= 128 to 300 days) and relatively immobile (mean K_{oc} 727 mL/g) in terrestrial environments. In aquatic environments, the environmental behavior of fipronil is more tentative because soil and aquatic metabolism studies provide contradictory data on fipronil persistence to microbially-mediated degradative processes. Major routes of dissipation appear to be dependant on photodegradation in water, microbially-mediated degradation, and soil binding. Fipronil degrades to form MB46136 and RPA 200766 in aerobic soil metabolism studies. MB46513 is a major degradate in photolysis studies. MB45950 appears to be predominantly formed under low oxygen conditions from microbial-mediated processes. These degradates appear to be persistent and relatively immobile in terrestrial and aquatic environments. Field dissipation studies confirm the persistence and relative immobility of fipronil and its degradates.

Water Resources Characterization

Because ground and surface water monitoring data are not available, drinking water concentrations for fipronil and its degradates are based solely on ground and surface water models. Acute and chronic drinking water concentrations for fipronil in surface water are not likely to exceed 0.715 and 0.276 µg/L, respectively. Based on the GENEEC model, acute and chronic drinking water concentrations of fipronil metabolites in surface water are respectively 0.168 and 0.062 µg/L for MB 46136, 0.014 and 0.009 µg/L for MB 46513, and 0.039 and 0.019 µg/L for MB 45950. Further refinement using a 36 year PRZM-EXAMS simulation suggest fipronil metabolites can potentially accumulate in surface water from 0.005 to 3.9 µg/L for MB 46513, 0.004 to 2.3 µg/L for MB45950, and 0.004 to 0.89 µg/L for MB46136.

The PRZM/EXAM modeling on the Yazoo, MS corn site is considered a very conservative runoff scenario because of the soil type (presence of a fragipan) and high rainfall conditions. Uncertainties in the surface water modeling are predominately associated with persistence of fipronil degradates in terrestrial and aquatic environments and fipronil persistence in aquatic environments. The PRZM-EXAMS modeling was conducted using the assumption that fipronil and its degradates are persistent in aquatic environments. This assumption was a conservative approach because of insufficient or contradictory metabolism data and was a factor in predictions of residue accumulation in surface waters (farm pond scenario). Additionally, the environmental fate data for MB46136 and MB45950 were taken from interim studies. Complete data submissions are needed to validate the environmental fate parameters for MB46136 and MB45950.

Based on the SCI-GRO model, acute drinking water concentrations in shallow ground water on highly vulnerable sites are not likely to exceed 0.055 µg/L for parent fipronil, 0.001 µg/L for MB 46136, 0.00026 µg/L for MB 46513, and 0.00036 µg/L for MB 45950. Because fipronil residues are moderately persistent to persistent in terrestrial environments, chronic concentrations of fipronil residues are not expected to be higher than acute values.

Because fipronil and its metabolites exhibit persistence and lower sorption affinity on coarse textured soils with low organic matter content, it possible that fipronil and it metabolites can move into shallow ground water on vulnerable sites. Moderate to high runoff areas in the major corn growing region (eastern two-thirds of the United States) are located in Ohio, southern Iowa and Illinois, and eastern Indiana, and the Gulf Coast of Texas. These have been identified as high runoff areas because of the high occurrence of Hydrologic Group C and D soils. It is important to note that runoff potential may also be affected by site specific management practices. Several highly vulnerable areas for shallow ground water have been identified as the coastal plains of Georgia, South Carolina, and North Carolina; eastern shore region of Lake Ontario; and the Delmarva Peninsula. Because several of these vulnerable areas are adjacent to estuarine environments, highly sensitive estuarine ecosystems may be potentially exposed to fipronil residues through surface water runoff or ground-surface water interactions.

Risks to Avian and Mammalian Receptors via Exposure to Fipronil in Granules

The terrestrial exposure for avian species is likely to be dependent on the in-furrow incorporation efficiency, granular dispersion processes, application timing, and the environmental persistence of fipronil in soil. In general, avian exposure is expected to greatest from direct ingestion of inadvertently exposed granules. However, the incorporation of granules into soil following applications of the REGENT formulations to corn is expected to mitigate dietary exposure to some extent. Actual granules, which are a point of major concern for avian safety, should disperse into the soil upon contact with moisture. The dispersion of the granule will likely be controlled by diffusion gradients from the granule surface. Therefore, the concentration of residues in soil are expected to be less uniform than with other formulations.

Granular exposures to fipronil for gallinaceous birds (e.g., quail, partridge, and pheasant) from in-furrow and T-band uses of granular formulations on corn exceed the criteria for restricted use. However, some songbird and waterfowl species appear to be less sensitive than gallinaceous birds and therefore are not felt to be at risk from corn use of fipronil. This risk assessment is based on single-dose oral toxicity studies with 6 species and dietary studies with 2 species. The potential impacts to avian species could be reductions in sensitive bird species populations (particularly gallinaceous species) in agricultural areas from oral ingestion of exposed granules, unearthed granules, and/or contaminated soils or soil organisms ingested through foraging activity. If acute impacts to bird populations from fipronil use do occur, they would be expected to concentrate during early spring months when corn is generally planted. The most sensitive avian species group tested for oral acute toxicity (quail, pheasant, and partridge) and dietary acute toxicity(quail) are also species commonly associated with agricultural production areas throughout the U.S. They are non-migratory and therefore potentially exposed throughout the growing season. Quail and other related species generally feed on seeds and insects which they often uncover by scratching the soil surface. There may be additional concerns regarding effects on a variety of migratory species potentially exposed if fipronil is applied with fall corn plantings. It is important to note that fipronil use on corn is restricted to a single at-plant application per season, regardless of when the crop is planted.

The assessment of risk to avian receptors from granular fipronil is based on ingestion of granules, the resultant risk quotients do not account for any exposure to fipronil degradates. It is anticipated that degradate residues from granular applications of fipronil would not be greater than encountered with in-furrow spray applications. Therefore, the potential for degradate risks to avian receptors for granular fipronil applications are not likely to be any greater than those estimated for in-furrow spray applications.

The absence of an EFED methodology for assessing risks to small mammals from ingestion of pesticides in granular formulation represents a considerable source of uncertainty to this risk assessment. Exposures of small mammals to granules not incorporated in soil cannot be quantified. The lack of quantified exposures via this route precludes assessment of risks to small mammals.

Risks to Avian and Mammalian Receptors via Exposure to Fipronil and Degradates in Soil and Soil Invertebrates (In-Furrow Spray)

Fipronil application by in-furrow spray will result in direct contact of the compound with soil particles. Because fipronil and it degradates exhibit persistence in laboratory and field dissipation studies, fipronil exposure may occur through ingestion of soil particles or soil invertebrates which have been coated by fipronil when applied as an in furrow spray. Several factors will control the concentrations of fipronil in soil and biotic compartments (e.g., soil invertebrate tissues) including aerobic soil metabolism, partitioning between soil and water, and volatilization. These properties were factored into the exposure assessment using an equilibrium partitioning (fugacity) model to estimate concentrations in soil and soil invertebrates. Because fipronil is applied during sensitive nesting and fledgling life stages of birds, the exposure potential will likely be higher. Quail species often forage in fields along with their young in the late spring or late summer (2nd clutch). Younger birds, therefore, are likely to be exposed to fipronil. Though data regarding sensitivity of younger gallinaceous species to fipronil is not available, it is expected that they may be more sensitive to an oral dosage than adult sized birds.

The actual physical exposure area in a given corn application site receiving in furrow spray nozzle application of fipronil is reduced to areas within or surrounding the actual furrow. However, this furrow area will contain a highly concentrated residue level since the per acre application rate is concentrated in the furrows. The incorporation of liquid sprays into soil can be expected to mitigate dietary exposure to some extent. Dietary exposures are expected to be at a maximum for bird and mammalian species that disturb or uncover soils in search of soil invertebrates. The most sensitive avian species for which toxicological data are available (quail, partridge, and the pheasant) are known to display this type of activity.

Comparisons of short-term dietary exposures to fipronil and its degradates to acute toxicological data suggest that the parent compound and degradates from in-furrow spray applications do not pose an acute risk to birds and mammals. However, the exposure estimates for avian and mammalian species do not include any exposure to fipronil or its degradates accumulated from soil through ingestion of vegetation. As vegetation may be an important dietary component in many avian and small mammal species, disgrading this exposure pathway represents a potential underestimation of risk.

Chronic dietary exposures for in-furrow spray applications of fipronil and associated degradates are based on average soil concentrations for the first 20-week period following year 1 of application. The models for these chronic exposure estimates conservatively assume that receptor organisms feed only in treated fields and consequently receive all incidental soil invertebrate prey exposure from the treated fields. The dietary exposure models assumed a depth-integrated concentration of fipronil or degradate at 15 cm as the appropriate interval for soil invertebrate exposure. In addition, soil ingestion of these compounds was assumed to occur with soils at a 1 cm depth; fipronil and degradate concentrations at this depth were factored into models of the incidental soil ingestion exposure route. Uncertainties associated with the percentage of prey and foraging occurring in treated fields cannot be quantified as many site specific factors (e.g., field size and geographical distribution) are likely to greatly influence the frequency and intensity of the use of treated corn fields as habitat.

The chronic dietary in-furrow spray assessment does not account for the potential for fipronil residue accumulation, particularly degradates, in soils from long-term repeated fipronil use. This would suggest that avian and mammalian exposure to fipronil and its degradates, and associated toxicological risk is underestimated, with respect to application years following the first year. Assuming that the degradates are of a high persistence ($t_{1/2}$ ca. 700 days) there remains the potential that repeated long-term use of fipronil would result in degradate soil concentrations exceeding first-year estimates. However, the degree to which the model underestimates exposure is uncertain as the model employed to assess accumulation over subsequent treatment years assumed in-furrow application to a fixed series of row locations in a given field. It is expected that actual furrow locations across a field will vary from year to year and therefore actual repetitive year accumulations may be lower than estimated by the existing model.

Another route of oral exposure not accounted for in the dietary exposure assessment is ingestion of fipronil dissolved in stormwater puddles on treated fields.

Because no clear chronic or reproductive effects profile (establishment of discrete NOEC and LOEC) has been determined for bobwhite or equally sensitive species at the expected environmental concentrations, potential chronic effects cannot be dismissed at this time. The available NOEC established at the highest dose tested (10 ppm) suggests that chronic hazard, if any gallinaceous birds may occur quite near the acute dietary thresholds suggested by the acute LC_{50} of 48 ppm. However, chronic test concentrations never exceeded 10 ppm. The LOEC for most sensitive bird species is uncertain at this time. Additionally, since fipronil metabolites (MB46136 and MB45950) contain the toxicological moiety (CF_3-) of parent fipronil and long-term exposure is anticipated because of high persistence in terrestrial environments, avian dietary studies are needed for MB46136 and MB45950.

A final uncertainty associated with dietary risks of fipronil and its degradates is the consideration of possible additive effects of exposure to combinations of the compounds. This risk assessment assumes that biologically active structural moieties in common between fipronil and degradates have similar toxicological potency. The logical extension to this structure/activity assumption is that compounds with common biologically active moieties may produce additive effects in organisms exposed to fipronil and toxic degradates. However, the magnitude of the effect of considering the combined toxic effects of fipronil and degradates cannot be determined at the present time because of incomplete comparative toxicological data.

Risks to Aquatic Organisms

Based on the presented for mysid shrimp, the most sensitive species tested, there is a high risk for chronic life-stage (reproductive) effects and moderate acute risk to estuarine invertebrates from use of fipronil use on corn. Because fipronil is extremely toxic to estuarine invertebrates and refined surface water modeling indicates surface water concentrations in excess of toxicity thresholds, a new mysid full life cycle (72-4) study with MB 46136 is needed to assess chronic effects on non-target aquatic invertebrates.

Although predicted GENEEC and PRZM-EXAMS EEC levels did not exceed the chronic levels of concern for rainbow trout, they are close enough to raise concerns for chronic effects to more sensitive fish species. The risk quotients for exposure to rainbow trout were based on fish early life stage toxicity data, not complete life cycle data. Therefore, there is a potential risk for direct chronic effects to both fresh and salt water fish species that may be more sensitive than the species and life stages that were toxicologically evaluated. Exposure of breeding fish populations may be more likely in early spring months for migratory fish species. The timing of fipronil applications would appear to correlate with these sensitive life stages. Also, since fipronil and its metabolites contain the same toxic moiety (CF_3-) and are persistent, a full fish life cycle study (72-5) is needed to assess cumulative toxicological impact on fish.

Aquatic exposure modeling for the fipronil degradates MB 46136 and MB 45950 indicates that EECs are not high enough to cause acute or chronic effects to freshwater invertebrates or fish. PRZM-EXAMS modeling indicates that fipronil degradates can accumulate in surface waters from corn use. This exposure assessment is based on interim data. Therefore, it is a preliminary assessment until the environmental fate data are completely reviewed and deemed acceptable by the Agency.

Uncertainties in the aquatic risk assessment are associated with the applicability of the GENEEC and PRZM/EXAMS model scenarios and the potential accumulation of fipronil degradates in estuarine environments. Estuarine environments are rarely isolated watersheds such as depicted by GENEEC and PRZM-EXAM modeling. Therefore, predicted EECs from GENEEC and PRZM-EXAMs are likely to be conservative because tidal dilution effects are not considered.

F. Recommendations for Label Revisions and Mitigation

Recommended mitigation options for in furrow use of fipronil are (1) restricted use classification and (2) label advisories. The registrant has volunteered to delete T-Band application methods from this proposed use to further mitigate risks to avian species.

Fipronil meets the criteria for classification as a **Restricted Use Pesticide** with regard to risks to estuarine invertebrates and birds (40 CFR 152.170 (c)(1)(iii)), and with regard to an avian acute oral toxicity value less than 50 mg/kg for a granular product (LD_{50} for Bobwhite Quail= 11.3 mg/kg) (40 CFR 152.170 (c)(2)(I)). EFED therefore recommends that fipronil be classified as a Restricted Use Pesticide.

Labels currently proposed contain language which is not consistent among products. EFED recommends that the label advisories for the environmental hazards statement for REGENT 1.5G, 3G, 80WG and 4SC use on corn should be consistent and include:

This pesticide is toxic to birds, fish, and aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Cover, incorporate or clean up granules that are spilled. Do not contaminate water when disposing of equipment washwater or rinsate.

Because of EFED's concern for estuarine organisms and because of the potential for accumulation of toxic residues in surface water receiving runoff from treated fields, EFED also recommends that the following precautions be incorporated into label language:

> Observe the following precautions when applying in the vicinity of aquatic areas:
>
> Do not apply within 20 yards of lakes, reservoirs, rivers, permanent streams, marshes, natural ponds, estuaries, commercial aquaculture facilities, or other bodies of water that convey water to these areas. (It is our understanding that this is consistent with the buffer established for corn cluster insecticides.)
>
> Protection of aquatic areas may be enhanced by maintaining all or a portion of this buffer in vegetative cover.

Environmental fate data suggest that fipronil and particularly its degradates are persistent in the environment. PRZM/EXAMS modeling incorporating these data indicate that under the proposed application to corn, fipronil and its degradates have the potential to accumulate in soil and surface water over multiple consecutive years of application. This can result in concentrations exceeding those estimated for the first year of application. Although these predictions are not highly refined, they do suggest that risks to aquatic organisms may increase over multiple consecutive years of application.

Because of persistence and possible accumulation of residues, EFED recommends that labels for all fipronil products registered for use on corn indicate that fipronil should not be applied to the same field in consecutive years. Alternating years of application may provide sufficient time for degradative processes to reduce the potential for residue accumulation in the environment.

The current status of environmental fate data requirements to support the registration of fipronil on terrestrial food and feed and terrestrial non-food crops (including turf) is as follows:

Environmental Fate Data Requirements	Status of Data Requirement	MRID No.
Degradation Studies-lab		
161-1 Hydrolysis (GML;06/15/94)	Fulfilled	42194701
161-2 Photodegradation in water (GML;06/15/94)	Fulfilled	42918661
161-3 Photodegradation on soil (GML;06/15/94)	Fulfilled	42918662
161-1 Photodegradation in air[1]		
Metabolism Studies-lab		
162-1 Aerobic soil (GML;06/15/94)	Fulfilled	42918663
162-2 Anaerobic soil[2]		
162-3 Anaerobic aquatic (GML;09/18/95)	Fulfilled	43291706 43291707
Mobility Studies		
163-1 Leaching, Adsorption/ Desorption (GML;06/15/94)	Fulfilled	42918664 43018801 44039003 00137544
163-2 Volatility-Lab[1]		
163-2 Volatility-Field[1]		
Dissipation Studies-field		
164-1 Soil (GML:09/18/95)	Fulfilled[3]	43291705 43401103

(GML;10/ /97)		44298001
Accumulation Studies		
165-4 in Fish	Fulfilled	43291706
(GML;09/18/95)		43291707
(GML;10/ /)		44298002
Spray Drift Studies		
201-1 Droplet size spectrum	Reserved[4]	
202-1 Drift field evaluation	Reserved[4]	

[1] Based on the low vapor pressure ($\approx 1 \times 10^{-7}$ mm Hg), volatility data is not needed at this time.

[2] An acceptable anaerobic aquatic metabolism study fulfills the anaerobic metabolism data requirement.

[3] The terrestrial field dissipation data requirement is fulfilled in-furrow applications and ground application (since the in-furrow application should be a worst case scenario) using the 1.5G and 80WG formulations at an application rate of ≤0.13 lb a.i./A. Additional terrestrial field dissipation data using different formulations may be needed to support the endproduct, higher application rate, and to make a complete environmental fate assessment fot higher application rates and/or different application methods.

[4] The spray drift data requirements (201-1 & 202-1) are reserved at this time. Spray drift data are needed according to 40 CFR §158.142 when aerial applications and/or ground applications (e.g. mist blower) are proposed and it is expected that the detrimental effect levels of non-target organisms present are exceeded. Members (Rhone-Poulenc is one) of the Spray Drift Task Force may satisfy this data requirement through the task force if neither EFED/EEB nor HED/TOX require these data in advance of the Task Force's final report.

Addendum:

Additional information from fipronil product labels is provided below.

Maximum seasonal rate for all 4 products is 0.13 pounds of active ingredient/acre.

80 WG
Apply at planting time as a solid stream using a microtube or other suitable metering orifice that is directed into the open seed furrow. Dilute REGENT 80WG Insecticide in a minimum of 1.5 gallon of water or water plus liquid fertilizer per acre. If flat fan nozzles are used for furrow application, the nozzles should be aligned with the row to direct spray into the open furrow.

4SC
Apply at planting time as a solid stream using microtube or other suitable metering device that is directed into the open seed furrow or to the side if the furrow at a distance not to exceed 2 inches over or 2 inches down. Dilute Regent 4SC Insecticide in a minimum of 0.5 gallon of water or liquid fertilizer per acre. If flat fan nozzles are used for in furrow application, the nozzles should be aligned with the row to direct spray into the open furrow.

1.5 G
At Planting
For Northern and Western Corn Rootworm Larvae Wireworms
Apply 0.5 lbs (8 oz) REGENT 1.5G per 1000 row feet.

Do not apply more than 8.7 lbs REGENT 1.5G per acre.

T-Band: Apply granules in a band 7 inches wide over or directly into an open seed bed furrow ahead of press wheel and lightly incorporate.

In-Furrow: Apply the granules directly into the seed furrow behind planter shoe and ahead of press wheel.

In-Furrow applications are recommended where wind or crop debris are likely to prevent proper placement of granules with a T-Band application.

When treating crops, granules lying on the soil surface in turn areas at row ends must be incorporated to remove possible hazards to birds and other wildlife.

3G label
T-Band: Apply granules in a band up to 7 inches wide over the press wheel or closure wheels and lightly incorporate into the top one inch of soil with suitable equipment.

In-Furrow: Apply the granules directly into the seed furrow behind the planter shoe and ahead of the press wheel.

In-furrow applications are recommended where wind or crop debris are likely to prevent proper placement of granules with a T-Band application.

Use Restrictions

80 WG label
Do not apply on row spacing less than 30 inches
Do not exceed 0.13 pounds of active ingredient or 2.6 ounces Regent 80WG per acre per season.
Do not apply to sweet corn or popcorn
Do not harvest within 90 days of application.
Do not plant leafy vegetables and root crops within five months following application.
Do not plant small grains or other rotational crops within 12 months following application.

1.5 G label
Do not feed treated corn or fodder to livestock.
Do not allow livestock to graze in treated fields.
Do not harvest within 90 days of application.
Do not apply this product in a way that will contact workers or other persons, either directly or through drift.

Make one application only during planting operation. Carefully calibrate granular application equipment to ensure accurate placement and rate.

For use on conventional or conservation tillage field corn systems.

Do not plant a cover crop for harvest, forage, or grazing following harvest of corn treated with REGENT 1.5G. Do not plant any crop other than field corn the year following REGENT 1.5G application.

3G Formulation
When treating agricultural crops, granules lying on the soil surface in turn areas at row ends must be incorporated to remove possible hazard to birds and other wildlife.

Make application only during the planting operation. Carefully calibrate granular application equipment to ensure accurate rate and placement.

For use on conventional and conservation tillage corn

Do not apply to sweet corn or popcorn.
Do not harvest within 90 days of application
Do not plant leafy vegetables within one month following application
Do not plant crops within five months following application
Do not plant small grains or other rotational crops within 12 months following application.
Do not apply more than 4.4 pounds of REGENT 3G Insecticide per acre

Regent 4SC
For use in conventional and conservation tillage corn.

Do not apply to sweet corn or popcorn.
Do not harvest within 90 days of application.
Do not plant leafy vegetables within one month following application.
Do not plant root crops within five months following application.
Do not plant small grains or other rotational crops within 12 months following application.
Do not apply to row spacing less than 30 inches.
Do not apply more than 0.13 lbs ai/acre or 4.2 fluid ounces of Regent 4 SC per acre.

G. References

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